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Proposed Registration Decision PRD2017-12

Cyclaniliprole and Cyclaniliprole 50SL Insecticide

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Overview

Proposed Registration Decision for Cyclaniliprole

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Technical Cyclaniliprole Insecticide and Cyclaniliprole 50SL Insecticide, containing the technical grade active ingredient cyclaniliprole, as a foliar insecticide to suppress or control various insect pests on a variety of vegetable, tree nut and fruit crops.

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

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 Technical Cyclaniliprole Insecticide and Cyclaniliprole 50SL 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. 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 the Canada.ca website at https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management.html.

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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."

Before making a final registration decision on cyclaniliprole and Cyclaniliprole 50SL Insecticide, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on cyclaniliprole and Cyclaniliprole 50SL Insecticide, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

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

What Is Cyclaniliprole?

Cyclaniliprole is a member of the diamide group of insecticides. Other insecticides in the same group registered in Canada are chlorantraniliprole and cyantraniliprole. Cyclaniliprole is the active ingredient in the end-use product Cyclaniliprole 50SL Insecticide, which suppresses or controls various insect pests on a variety of vegetable, tree nut and fruit crops.

Health Considerations

Can Approved Uses of Cyclaniliprole Affect Human Health?

Cyclaniliprole 50SL Insecticide, containing cyclaniliprole, is unlikely to affect your health when used according to label directions.

Potential exposure to cyclaniliprole may occur through the diet (food and water), when handling and applying the product, or when entering an area that has been treated with 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). 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, the technical grade active ingredient (TGAI) cyclaniliprole was of low acute toxicity via the oral, dermal and inhalation routes. It was non-irritating to the skin and eyes and did not cause an allergic skin reaction. Based on these findings, hazard statements for acute toxicity are not required on the label.

The end-use product, Cyclaniliprole 50SL Insecticide, was of low acute toxicity via the oral, dermal, and inhalation routes of exposure. It was minimally irritating to the eyes and not irritating to the skin. It did not cause an allergic skin reaction. Based on these findings, hazard statements for acute toxicity are not required on the label.

Registrant-supplied short-term and long-term (lifetime) animal toxicity tests were assessed for the potential of cyclaniliprole to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, genetic damage, and various other effects. The most sensitive endpoints for risk assessment included marginal effects on the liver. There was no evidence that the young were more sensitive to cyclaniliprole than the adult animal.

The risk assessment protects against the effects noted above 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

Dietary risks from food and drinking water are not of health concern.

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and children 1-2 years old, the subpopulation which would ingest the most cyclaniliprole relative to body weight, are expected to be exposed to a maximum of 5% of the acceptable daily intake (ADI). Based on these estimates, the chronic dietary risk from cyclaniliprole is not of health concern for all population subgroups.

Animal studies revealed no acute health effects. Consequently, a single dose of cyclaniliprole is not likely to cause acute health effects in the general population (including infants and children).

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.* Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using cyclaniliprole on representative crops of leafy vegetables (crop group 4-13), brassica head and stem vegetables (crop group 5-13), fruiting vegetables (crop group 8-09), cucurbit vegetables (crop group 9), pome fruit (crop group 11-09), stone fruit (crop group 12-09), small fruits vine climbing crop subgroup, except fuzzy kiwifruit (crop subgroup 13-07f) and tree nuts (crop group 14-11) are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of this document.

Risks in Residential and Other Non-Occupational Environments

Residential and non-occupational risks are not of concern when Cyclaniliprole 50SL Insecticide is used according to the proposed label directions.

Given that fruits and berries can be treated with cyclaniliprole, there is potential for exposure from pick-your-own activities. Health risks from these activities have been evaluated and are not of concern.

Occupational Risks From Handling Cyclaniliprole 50SL Insecticide

Occupational risks are not of concern when Cyclaniliprole 50SL Insecticide is used according to the approved label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Cyclaniliprole 50SL Insecticide as well as field workers re-entering freshly treated fields and orchards can come in direct contact with cyclaniliprole residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Cyclaniliprole 50SL Insecticide must wear a long-sleeved shirt, long pants, shoes, socks and chemical-resistant gloves (chemical-resistant gloves are not required during groundboom or aerial application). The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the health risk to these individuals are not of 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 Cyclaniliprole Is Introduced Into the Environment?

When used according to label directions, cyclaniliprole is not expected to pose risks of concern to the environment.

Cyclaniliprole enters the environment when applied to control or suppress insect pests on certain vegetable, tree nut or fruit crops. It can remain in the environment for a long time as it does not break down in the presence of water or soil. In the presence of sunlight, it can break down to form several breakdown products, but these are not expected to persist in the environment. Cyclaniliprole is not expected to move into the air from water or moist soils. It is not expected to accumulate in the tissues of organisms. Cyclaniliprole is not expected to move inside plants and its residues will remain mostly on leaves; spray application during bloom may result in residues on the flowers.

Cyclaniliprole does not present a risk of concern to wild mammals, birds, fish and amphibians. Cyclaniliprole may affect bees and beneficial insects if these are exposed to high enough levels. Freshwater and marine invertebrates may also be affected by exposure in surface water as a result of spray drift. To minimize exposure and reduce risks to these organisms, use restrictions, spray buffer zones and precautionary label statements are required.

Some cyclaniliprole can still be found in the soil the next growing season after it is applied and it has the potential to move through soil to reach groundwater; therefore, precautionary label statements are required to inform users that cyclaniliprole can persist in soil and reach groundwater.

Value Considerations

What Is the Value of Cyclaniliprole 50SL Insecticide?

Cyclaniliprole 50SL Insecticide is a new tool to control or suppress various insect pests on many outdoor crops and represents a new mode of action for resistance management on certain crop-pest combinations.

Cyclaniliprole 50SL Insecticide is a new product which is applied as a foliar spray to control or suppress various insect pests on labelled vegetable, tree nut and fruit crops. It can be applied by ground application to all listed crops, and by aerial application to the vegetable crops. While other diamide products are registered for most of the uses of Cyclaniliprole 50SL Insecticide, it is the first insecticide proposed for registration in Canada to control walnut husk fly on stone fruits, and omnivorous leafroller on stone fruits and small fruits (vine climbing) other than grapes. Cyclaniliprole also represents a new mode of action for certain crop-pest combinations including use on small fruits (vine climbing) against spotted wing drosophila, an invasive pest which is difficult to control, and will therefore be useful for resistance management on these crop-pest combinations.

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 Cyclaniliprole 50SL Insecticide 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 cyclaniliprole on the skin or through inhalation of spray mists, anyone mixing, loading and applying Cyclaniliprole 50SL Insecticide must wear a long-sleeved shirt, long pants, shoes, socks and chemical-resistant gloves (chemical-resistant gloves are not required during groundboom or aerial application). In addition, standard label statements to protect against drift during application were added to the label. The label also requires that workers do not enter treated fields for 12 hours after application.

Environment

Precautionary label statements are required to inform users of the potential risks of carry-over and leaching of cyclaniliprole.

To minimize exposure and reduce risks to bees, beneficial arthropods and aquatic invertebrates, use restrictions, spray buffer zones and precautionary label statements are required. Application is restricted to periods when most bees are not actively foraging, and/or when flowers are closed. In addition, application is restricted during the blooming period of crops that are highly attractive to bees such as pome fruits and stone fruits, or when managed bees are used for pollination services.

Next Steps

Before making a final registration decision on cyclaniliprole and Cyclaniliprole 50SL Insecticide, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

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

What Additional Scientific Information is Being Requested?

Chemistry

Since this technical product is only manufactured at pilot scale before registration, five-batch data representing commercial-scale production at all listed manufacturing sites will be required as post-market information after registration.

Science Evaluation

Cyclaniliprole

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance

Function Insecticide

Chemical name

1. **International Union of Pure and Applied Chemistry (IUPAC)** 2′,3-dibromo-4′-chloro-1-(3-chloro-2-pyridyl)-6′-{[(1*RS*)-1-cyclopropylethyl]carbamoyl}pyrazole-5-carboxanilide

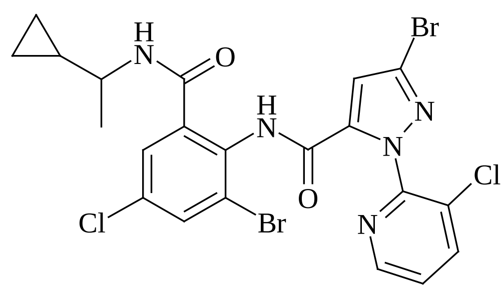
2. **Chemical Abstracts Service (CAS)** 3-bromo-*N*-[2-bromo-4-chloro-6-[[(1-cyclopropylethyl)amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide

CAS number 1031756-98-5

Molecular formula $C_{21}H_{17}Br_2Cl_2N_5O_2$

Molecular weight 602.1

Structural formula



Purity of the active ingredient 96.4%

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

Technical Product—Technical Cyclaniliprole Insecticide

Property	Result
Colour and physical state	White solid
Odour	No odour

Property	Result
Melting range	241 - 244°C
Boiling point or range	Not applicable
Relative density	1.6
Vapour pressure at 20°C	2.4×10^{-6} Pa at 25°C
Henry's law constant at 20°C	9.5×10^{-8} atm m^3/mole
Ultraviolet (UV)-visible spectrum	Medium (pH) / λ_{max} (nm) / Absorbance (a) / ε (dm^3/mol/cm) Purified water (pH 6.4) / 229.5 (sh) / 0.6508 / 25020 271.6 (sh) / 0.3657 / 14060 0.1 M aqueous HCl (pH 1.1) / 203.7 / 0.8260 / 31760 229.4 (sh) / 0.5219 / 20070 270.9 (sh) / 0.2847 / 10950 0.1 M aqueous NaOH (pH 13.2) / 246.7 (sh) / 0.5333 / 20500 272.3 (sh) / 0.3381 / 13000 316.0 (sh) / 0.1074 / 4129 (a) Concentration 15.66 mg/L (sh) = shoulder No absorption above 400 nm
Solubility in water at 20°C	0.12 mg/L in pH 5 buffer 0.10 mg/L in pH 7 buffer 0.18 mg/L in pH 9 buffer
Solubility in organic solvents at 20°C	Solvent / Solubility (g/L) n-Heptane 0.0001 Xylene 0.20 1,2-Dichloroethane 4.4 Acetone 10 Methanol 4.0 n-Octanol 1.5 Ethyl acetate 3.6
n-Octanol-water partition coefficient (K_{ow})	pH / log K_{ow} 5 2.8 7 2.4 9 2.0
Dissociation constant (pK_a)	$pK_a = 8.6$
Stability (temperature, metal)	Stable in contact with aluminium, aluminium acetate, iron, iron acetate, zinc and zinc acetate, and at elevated temperatures when stored at 54°C for 14 days.

End-Use Product—Cyclaniliprole 50SL Insecticide

Property	Result
Colour	Yellow transparent
Odour	Chemical odour
Physical state	Liquid
Formulation type	Suspension
Guarantee	50 g/L
Container material and description	Plastic bottles and drums 500 mL – 200 L
Density	1.1 g/mL
pH of 1% dispersion in water	5.03
Oxidizing or reducing action	N/A
Storage stability	The product was shown to be stable when stored for two years at 20°C ± 2°C in HDPE bottle.
Corrosion characteristics	Not corrosive to the container material.
Explodability	Not explosive.

1.3 Directions for Use

Cyclaniliprole 50SL Insecticide is applied as a foliar spray to control or suppress a variety of insect pests on labelled vegetable, tree nut and fruit crops. Application rates are 0.8-1.2 L/ha for the vegetable crops, and 1.2-1.6 L/ha for the tree nut and fruit crops. Cyclaniliprole 50SL Insecticide can be applied to all listed crops by ground application and to the vegetable crops by aerial application. The higher rate is to be used when pest pressure is high and/or when the crop canopy is dense. See Appendix I, Table 25 for details.

1.4 Mode of Action

Cyclaniliprole is a diamide insecticide in Group 28 of the Insecticide Resistance Action Committee (IRAC) Mode of Action Classification. Diamides modulate the ryanodine receptors of insects. Insects which ingest or contact cyclaniliprole become paralysed, stop feeding and die. Cyclaniliprole has translaminar activity when applied as a foliar treatment.

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 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

High performance liquid chromatography methods with tandem mass spectrometric detection (HPLC-MS/MS; Method JSM0269 in plant matrices and Method JSM0277 in animal matrices) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70-120%) were obtained in plant and animal matrices. The proposed enforcement methods were successfully validated in plant and animal matrices by an independent laboratory. Adequate extraction efficiencies were demonstrated using radiolabelled samples of crop and animal matrices analyzed with the enforcement method. Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Cyclaniliprole belongs to the anthranilic diamide class of pesticides. Pesticides of this class control insects through unregulated activation of ryanodine receptor channels, leading to internal calcium store depletion that impairs regulation of muscle contraction. Mammalian ryanodine receptors are substantially less sensitive to the effects of anthranilic diamides than the insect ryanodine receptors.

A detailed review of the toxicological database for cyclaniliprole was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices (GLP). The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to cyclaniliprole.

Toxicokinetic data consisted of studies in which rats were administered single low or high gavage doses, or repeated low gavage doses of ^{14}C-cyclaniliprole radiolabeled in either the phenyl ring or pyrazole position. Toxicokinetic data were also available for dogs following administration of a single low dose using both radiolabels. In both species, the position of the radiolabel did not have a significant impact on the toxicokinetic profile.

In rats, absorption was low (approximately 10% of the administered dose [AD] after 48 hours) following a single low dose, and even lower following administration of a single high dose. The majority of the AD was eliminated quickly in both doses, mostly via the feces. Only a small portion of the AD was excreted via the urine and bile. Radioactivity was not detected in respired air. The pattern of absorption and excretion was not altered following repeat dosing.

Following single dosing in rats, plasma concentration peaked and remained elevated after 24 hours, with higher levels in males than females. Levels of radioactivity in plasma were dose-dependent, but did not increase linearly. Following repeat dosing, extensive accumulation of radioactivity occurred in plasma and whole blood. Plasma concentrations did not reach equilibrium after 14 days of dosing. After dosing cessation, terminal half-lives could not be calculated since levels of radioactivity did not decline significantly in the post-dosing period (up to 168 hours).

After administration of a single dose in rats, highest tissue radioactivity concentrations were noted in plasma and whole blood, followed by the liver, lungs, adrenals, fat, thyroid, and ovaries or epididymides. Terminal tissue concentrations were similar between males and females. Overall, tissue accumulation was low after 168 hours. Tissue concentrations did not decrease significantly over time (168 hours), with the exception of the gastro-intestinal (GI) tract and liver. Following repeat low dosing in rats, tissue concentrations were up to 40-fold higher than those following single low dosing.

Cyclaniliprole was not extensively metabolized, with the majority of the AD eliminated via the feces as unchanged cyclaniliprole. It was not detected in urine or bile, and only represented a small portion of the radioactivity found in plasma. The proposed metabolic pathway for cyclaniliprole proceeds via hydrolysis of the amino-cyclopropane bond, yielding YT-1284. YT-1284 then either undergoes oxidative deamination at the carboxylic amide of the phenyl ring, producing NSY-27, or alternatively, condensation or tautomerization, yielding NSY-28. The metabolites NSY-27, NSY-28 and YT-1284 were identified in bile/urine, in each case accounting for less than 1% of the AD. NSY-28 was the major metabolite in plasma and kidney. In liver and fat, the majority of the radioactivity was in the form of unchanged cyclaniliprole. NK-1375, another metabolite, was also found in the fat. (See Table 2 of Appendix I for common names of the metabolites).

When beagle dogs received a single low dose of radiolabelled cyclaniliprole, absorption ranged from 30 to 49% of the AD after 48 hours. Excretion was incomplete after 48 hours (27 to 47% of AD excreted) and occurred mainly via the feces. As in rats, only a small portion of the AD was excreted via the bile and urine. Radioactivity in plasma, blood and organs was lower in females than in males. Peak plasma concentration occurred between 6 and 48 hours, with some animals not reaching peak concentration before study termination. As was the case in rats, the plasma half-life was not determined as levels of radioactivity did not decline during the study. The highest concentrations of radioactivity were noted in the plasma, whole blood, liver and fat. Significant amounts of radioactivity were found in the carcass. Overall, the study utility was limited by the low number of animals, high inter-animal variability, and the fact that the study was terminated 48 hours post-dosing.

When tested in the rat, cyclaniliprole was of low acute toxicity via the oral, dermal, and inhalation routes of exposure. It was not irritating to the skin and eyes of rabbits and it was not a skin sensitizer when tested on guinea pigs (Maximization method) and mice (LLNA).

The end-use product, Cyclaniliprole 50SL Insecticide, was of low acute toxicity in rats via the oral, dermal, and inhalation routes of exposure. It was not irritating to the skin and minimally irritating to the eyes of rabbits and it was not a skin sensitizer when tested on guinea pigs (Buehler method) and mice (LLNA).

Repeat-dose dietary toxicity studies with cyclaniliprole in mice, rats, and dogs revealed the liver as the target organ of toxicity. Study duration did not have an impact on toxicity. In rodents, the liver findings were minimal (increased liver weights) and considered adaptive and non-adverse, occurring at doses approaching or exceeding the limit dose of testing. Reduction of total bilirubin was also noted in rats. Dogs were slightly more sensitive to the liver effects than rodents, with findings occurring in the 90-day and 1-year studies at lower dose levels. With increasing dose, the effects on liver weight in dogs in these studies became more pronounced and were accompanied by hepatocellular hypertrophy, increased alkaline phosphatase and decreased blood albumin levels. Higher doses could have been used in the dog studies and the effects showed a fairly flat dose response, possibly due to limited absorption. Overall, the liver effects in dogs at the highest doses in both studies were considered adverse, although it is recognized that this may represent a conservative interpretation.

No toxicity or signs of dermal irritation were noted following short-term exposure to cyclaniliprole via the dermal route in rats at the limit dose of testing. A repeated-exposure inhalation toxicity study was not conducted. A waiver for this data requirement for the petitioned uses was accepted on the basis of the low acute toxicity, low overall toxicity in the cyclaniliprole toxicology database, and the margins of exposure calculated when using a toxicological endpoint from an oral toxicity study.

There was no evidence of carcinogenicity in rats or mice following long-term dietary exposure with cyclaniliprole. Results of a battery of in vitro and in vivo genotoxicity tests did not suggest genotoxic potential.

Gavage developmental toxicity studies in rats and rabbits and a dietary two-generation reproductive toxicity study in rats did not demonstrate toxicity to the reproductive system, the parental animal, the developing fetus or young animal at dose levels that were at, or above, the limit dose of testing.

There was no evidence of neurotoxicity in acute and subchronic oral neurotoxicity studies conducted in rats at the limit dose of testing.

In a short-term dietary immunotoxicity study in rats, a non-statistically significant decrease in Plaque-Forming Colonies (PFC)/10^6 spleen cells was observed at the highest dose tested. The high variability in the data confounded interpretation, and therefore these findings were considered equivocal. There was a low level of concern, however, based on the fact that they were observed at a dose well in excess of the limit dose of testing, and there was no other indication of immunotoxicity in the overall database. The study no observable adverse effect level (NOAEL) was thus established at the highest dose tested.

An acute oral toxicity study in rats and a gene mutation assay in bacteria were conducted with NK-1375, a photodegradate of cyclaniliprole. NK-1375 was also identified in the toxicokinetic investigations in rats. The studies indicated that NK-1375 was of low acute oral toxicity and negative in the gene mutation assay.

Results of the toxicology studies conducted on laboratory animals with cyclaniliprole and its associated end-use product are summarized in Appendix I, Tables 3 and 4. The toxicology endpoints for use in the human health risk assessment are summarized in Appendix I, Table 5.

Incident Reports

Cyclaniliprole is a new active ingredient pending registration for use in Canada and the United States. As such, no incident reports have been received by the PMRA.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the standard complement of required studies, including oral gavage developmental toxicity studies in rats and rabbits and a dietary two-generation reproductive toxicity study in rats, was available for cyclaniliprole.

With respect to potential prenatal and postnatal toxicity, no adverse effects were observed in the developing young, offspring, or adult animal in the developmental toxicity studies or the reproductive toxicity study when tested at dose levels up to, or exceeding, the limit dose of testing. Effects in the young were well-characterized in these studies.

On the basis of the above information, the *Pest Control Products Act* factor was reduced to 1-fold.

3.2 Acute Reference Dose (ARfD)

An ARfD was not established as no effect attributable to a single exposure to cyclaniliprole was identified in the toxicology database.

3.3 Acceptable Daily Intake (ADI)

To estimate risk from repeated dietary exposure, the overall NOAEL of 27 mg/kg bw/day from the combined results of the 90-day and 1-year dog dietary studies was selected as the point of departure (POD). At the respective 90-day and 1-year study lowest observed adverse effect levels (LOAELs) of 266 and 259 mg/kg bw/day, increased liver weights, hepatocellular hypertrophy, increased alkaline phosphatase, and decreased albumin were observed. These studies provide the lowest NOAEL in the database, and selection of this endpoint is considered to be protective of all populations. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. **The composite assessment factor (CAF) is thus 100.**

The ADI is calculated according to the following formula:

$$ADI = \frac{NOAEL}{CAF} = \frac{27 \text{ mg/kg bw/day}}{100} = 0.3 \text{ mg/kg bw/day of cyclaniliprole}$$

Cancer Assessment

There was no evidence of carcinogenicity; therefore, a cancer risk assessment was not necessary.

3.4 Occupational Risk Assessment

3.4.1 Toxicological Endpoints

Occupational exposure to cyclaniliprole is characterized as short- to intermediate-term and is predominantly by the dermal and inhalation route.

Short- and Intermediate-term Dermal

For the short- and intermediate-term dermal risk assessment, the NOAEL of 1000 mg/kg bw/day from the 28-day dermal toxicity study in rats was selected as the POD. The choice of this study was supported by the overall low level of toxicity in the cyclaniliprole toxicology database, including the absence of developmental, reproductive, or offspring toxicity as well as neurotoxicity at, or above, the limit dose of testing. In addition, there was no indication of increased toxicity with increased duration of dosing in the database.

The target Margin of Exposure (MOE) is 100, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of this POD and MOE is considered to be protective of all populations, including nursing infants and unborn children.

Short- and Intermediate-term Inhalation

For the short- and intermediate-term inhalation risk assessment, the NOAEL of 27 mg/kg bw/day from the 90-day dog dietary study was selected as the POD. At the LOAEL of 266 mg/kg bw/day, increased liver weights, hepatocellular hypertrophy, increased alkaline phosphatase, and decreased albumin were observed.

The target MOE is 100, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of this POD and MOE is considered to be protective of all populations, including nursing infants and unborn children.

3.4.1.1 Dermal Absorption

In support of the registration of Cyclaniliprole 50SL Insecticide, an in vivo dermal absorption study in rats and two in vitro dermal absorption studies in rat and human skin were submitted. Together, these studies are referred to as a ‘triple pack’. The dermal penetration studies for cyclaniliprole were of good quality and the ‘triple pack’ approach was considered for setting a dermal absorption value.

In the in vivo dermal absorption study, radiolabelled cyclaniliprole formulated as a liquid formulation was applied dermally to groups of male rats at two dose levels corresponding to the commercially available formulation (nominally 50 g a.i./L, high dose) and an in-use rate of the product (0.1 g a.i./L, intermediate dose). Five groups of male rats (each group consisted 4-7 rats) per dose level received a six-hour topical exposure of cyclaniliprole. After exposure, the test material was washed off and groups of rats were sacrificed at 6, 24, 72, 120 and 168 hours after application. Following sacrifice, the treated skin was tape-stripped to remove the stratum corneum. Radioactivity in excreta, cage wash, skin washings, tape-strips, residual skin and remaining carcass was determined by liquid scintillation counting (LSC). The amount of radioactivity absorbed, excreted, and present on or in the skin was calculated.

In the in vitro dermal absorption studies, radiolabelled cyclaniliprole formulated as a liquid formulation was applied on excised rat and human skin. Cyclaniliprole was applied at three dose levels corresponding to the commercially available formulation (nominally 50 g a.i./L, high dose) and two lower, in-use rates of the product (0.1 and 0.01 g a.i./L). The skin samples were exposed to the test material for six hours, after which time the remaining dose was washed off the skin with a mild detergent solution. Receptor fluid samples were collected at hourly or two-hourly intervals for the duration of the experiment (24 hours). At the end of the experiment, the skin samples were tape-stripped to remove residual surface dose and stratum corneum. The distribution of radioactivity in the skin was determined by LSC of the various samples collected.

Dermal absorption values from the in vivo study included the % dose absorbed, excluding in skin bound residues, since absorption was essentially complete by 72 hours. In the in vitro studies, absorption was <75% at the midpoint of the high and low level tests; therefore, it was considered that material remaining in the stratum corneum may be available for absorption and should be included in the dermal absorption calculation. Tables 3.4.1.1-1 and 3.4.1.1-2 present the in vivo and in vitro dermal absorption values after 6 hours of exposure.

Table 3.4.1.1-1 Dermal absorption values (% of total dose applied) from the in vivo rat study, 6 hours exposure

Dose level	Sacrifice time				
	6 hours	24 hours	72 hours	120 hours	168 hours
High (512 μg/cm^2)	1.1	1.7	2.8	1.0	0.9
Intermediate (1.1 μg/cm^2)	1.3	1.1	1.1	1.1	1.3

Dermal absorption (% of total dose applied) = radioactivity recovered from urine, faeces, cage wash, skin samples (excluding stratum corneum and surface skin strips) and carcass

Table 3.4.1.1-2 Dermal absorption values (% of total dose applied) from the in vitro rat and human studies; 6 hours exposure, 24-hour study duration

Dose level[1]	High	Intermediate	Low
% Absorption - rat skin	10.0	10.6	19.9
% Absorption - human skin	2.2	8.2	14.1

Dermal absorption (% of total dose applied) is radioactivity in the receptor fluid and dose remaining in skin.
[1] Actual doses for in vitro rat: 513, 1.1 and 0.11 µg/cm^2. Actual doses for in vitro human: 408, 0.9 and 0.09 µg/cm^2.

To use the triple pack approach, the ratio of the in vitro to the in vivo dermal absorption factors from the animal studies must be close to 1, which indicates that a human in vitro study conducted under the same conditions as the animal test is likely to be a good predictor of human dermal absorption. In addition, the usefulness of the dermal absorption data would necessarily be dependent on the validity and applicability of the experimental design as well as consideration of the 'minimal standards' discussed in the "NAFTA Dermal Absorption Position Paper on Use of in vitro Dermal Absorption Data in Risk Assessment".

Table 3.4.1.1-3 compares the % of applied dose that was absorbed after 6 hours exposure (24 hours study duration) for high, intermediate and low doses in the rat studies. The % of applied dose that was dermally absorbed from the in vitro rat study is similar to that from the in vivo rat study at the intermediate dose, but not very similar at the high dose (ratio of in vitro to in vivo absorption in rats = 1.2 and 3.4 for intermediate dose and high dose, respectively). In addition, as shown in the in vivo study, absorption is complete after 72 hours, which the in vitro study could not determine. Thus, the 24-hour study duration is not fully representative of how the chemical is absorbed. As such, the in vitro rat dermal absorption study was not considered to be a good predictor of rat dermal absorption in vivo.

Table 3.4.1.1-3 Comparison of % of applied dose absorbed from in vivo and in vitro rat studies for cyclaniliprole following 6 hours of exposure, 24 hours study duration

Dose level[1]	% of applied dose absorbed[2]		Ratio
	Rat in vitro	**Rat in vivo**	**in vitro rat / in vivo rat**
High	10.0	2.9	3.4
Intermediate	10.6	9.1	1.2
Low	19.9	N/A	N/A

[1] Actual doses for in vitro rat: 513, 1.1 and 0.11 µg/cm^2. Actual doses for in vivo rat: 512 and 1.1 µg/cm^2.
[2] % of applied dose absorbed calculated for:

- Rat in vitro = receptor fluid + receptor chamber + skin (including tape strips and stratum corneum)
- Rat in vivo = treated skin (including stratum corneum) + urine + feces + cage wash + blood + non-treated skin + carcass
  Skin bound residues were included because absorption was not completed by 24 hours

N/A = not available

Due to the results in the in vitro study, the dermal absorption values derived from the in vitro human dermal absorption data cannot be used for human health risk assessments. As such, the in vivo rat dermal absorption data are used to derive the dermal absorption value used for risk assessment purposes. As per the OECD guidance notes, the dermal absorption value from the final time point in the study was chosen to be the most appropriate regulatory value, as the fate of residues can be more adequately characterized. At 6-hour exposure and 168-hour sacrifice (1.1 µg/cm^2), dermal absorption in the in vivo rat study was 1.3% of the applied dose. A dermal absorption value of 2% (rounded from 1.3%) is deemed appropriate, as the in vivo study was conducted at 6 hours (compared to the 8-hour exposure for workers). In addition to the dermal absorption data, the low dermal absorption value for cyclaniliprole is supported by its physical-chemical properties including a high molecular weight (602.1 g/mol), low solubility in water (0.15 mg/L) and high solubility (high lipophilicity) in octanol (1.4 g/L). Based on these physical-chemical properties, cyclaniliprole is not expected to be highly absorbable, which is consistent with what is observed in the three dermal absorption studies.

A dermal absorption factor of 2% was established for cyclaniliprole for risk assessment purposes. However, it was not used in the occupational risk assessment since the short- to intermediate-term dermal endpoint is based on a dermal toxicity study.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to cyclaniliprole during mixing, loading and application. Exposure to workers mixing, loading and applying cyclaniliprole is expected to occur primarily by the dermal and inhalation routes for a short- to intermediate-term duration. Exposure estimates were derived for mixers/loaders/applicators applying cyclaniliprole to leafy vegetables, brassica head and stem vegetables, fruiting vegetables and cucurbit vegetables while using groundboom equipment. Exposure estimates were also derived for mixer/loaders/applicators applying cyclaniliprole to pome fruit, tree nuts, stone fruit and small vine climbing fruits (except fuzzy kiwifruit) using airblast equipment. In addition, exposure estimates were derived for mixers/loaders/applicators applying cyclaniliprole to leafy vegetables, brassica head and stem vegetables and cucurbit vegetables using aerial equipment. The exposure estimates are based on mixers/loaders/applicators wearing a long-sleeved shirt, long pants, shoes, socks and chemical-resistant gloves.

As chemical-specific data for assessing human exposures during pesticide handling activities were not submitted, dermal and inhalation exposure estimates for workers were generated using the Pesticide Handlers Exposure Database (PHED), version 1.1 (for groundboom and aerial application) and the Agricultural Handlers Exposure Task Force (AHETF) (for airblast application).

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. The dermal absorption was not used in the calculation of dermal exposure, since the short- to intermediate-term dermal endpoint is based on a dermal toxicity study.

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 80 kg adult body weight.

Exposure estimates were compared to the toxicological endpoints (NOAELs) to obtain the MOE; the target MOE is 100. Dermal and inhalation MOEs were not combined, since the dermal and inhalation endpoints are not based on the same toxicological effects. Calculated MOEs are above the target MOE of 100 for all chemical handler scenarios.

Table 3.4.2.1-1 Mixer/loader/applicator risk assessment for Cyclaniliprole 50SL Insecticide for chemical handlers wearing a single layer (and gloves when mixing/loading and when applying with airblast equipment)

Exposure scenario	Unit exposure (µg/kg a.i. handled)[1]		ATPD (ha/ day)[2]	Rate (kg a.i./ ha)	Daily exposure (mg/kg bw/day)[3]		Margin of exposure[4]	
	Dermal	Inhal			Dermal	Inhal	Dermal	Inhal
Groundboom - Farmer and Custom	84.12	2.56	26	0.060	0.00164	0.0000499	610,000	541,000
Airblast	3820.44	10.68	20	0.080	0.0764	0.000214	13,100	126,000
Aerial M/L	51.14	1.60	400	0.060	0.0153	0.00048	65,200	56,200
Aerial App	9.66	0.07	400	0.060	0.00290	0.000021	345,000	1,290,000

Inhal = inhalation, M/L = mixer/loader, App = applicator

[1] Unit exposure values from PHED (groundboom and aerial) and AHETF (airblast).

[2] Default area treated per day (ATPD) values

[3] Daily exposure = (PHED/AHETF unit exposure x ATPD x Rate) / (80 kg bw x 1000 µg/mg)

[4] Based on Dermal NOAEL = 1000 mg/kg bw/day, target MOE = 100 and
Inhalation NOAEL = 27 mg/kg bw/day, target MOE = 100

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers entering areas treated with cyclaniliprole while performing activities such as scouting, handset irrigation, hand weeding, hand harvesting, thinning, girdling and turning. The duration of exposure is considered to be short- to intermediate-term for all uses. The primary route of exposure for workers re-entering treated areas would be through the dermal route. Inhalation exposure is not considered to be a significant route of exposure for people entering treated areas compared to the dermal route, since cyclaniliprole is relatively non-volatile (2.4×10^{-9} kPa at 25°C) and as such, an inhalation risk assessment was not required.

Dermal exposure to workers entering treated areas is estimated by coupling dislodgeable foliar residue values with the highest activity-specific transfer coefficient (TC) for each crop group. Activity TCs are based on Agricultural Re-entry Task Force (ARTF) data. As such, the risk assessment covers off all the crops and its associated activities, including hand harvesting.

Chemical-specific dislodgeable foliar residue (DFR) data were submitted. Three DFR studies were conducted on squash, apple and grape. The squash DFR study was conducted at three test sites in North Carolina, North Dakota and California. Each treatment plot received three foliar broadcast spray applications of the test substance via handheld boom/backpack sprayer or a tractor-mounted sprayer at a nominal application rate of 0.080 kg a.i./ha/application (total seasonal rate of 0.240 kg a.i./ha), at a retreatment interval of 6-8 days. The apple DFR study was conducted in New York, Illinois and Washington with each treatment plot receiving three foliar broadcast spray applications of the test substance via airblast sprayers at a nominal application rate of 0.100 kg a.i./ha at a retreatment interval of 13-15 days, for a total seasonal application rate of 0.300 kg a.i./ha/season. The grape DFR study was conducted in California, Washington and Pennsylvania. Each treatment plot received three or four foliar broadcast spray applications of the test substance via airblast sprayers at a nominal rate of 0.100 kg a.i./ha/application. Three applications were made at the California and Washington test sites, for a total seasonal application rate of 0.300 kg a.i./ha/season. Four applications were made at the Pennsylvania site for an actual seasonal application rate of 0.400 kg a.i./ha/season. Applications were made at a retreatment interval of 7 days, with the exception of the third application at the Pennsylvania site which was made at a retreatment interval of 13 days.

For all test sites, triplicate control plot and treated plot DFR samples were collected using a Birkestrand leaf punch sampler prior to the first application, prior to the final application, and at intervals following the final application (1 and 8 hours, and 1, 2, 3, 4-5, 9-11, 13-15, 20-21, 28 and 34-36 days). DFR values were corrected for field recoveries less than 95%. For residues reported as below the limit of quantification (LOQ), ½ LOQ was used in the calculations. First-order dissipation kinetics were assumed to generate dissipation curves for cyclaniliprole.

The DFR study results were compared in each site, and the climate of study sites and representative Canadian sites were also compared. All sites were determined to be representative of Canadian growing regions. As such, the DFR values from the trial sites which yielded the most conservative DFR estimates were used in the risk assessment:

- 28% of the application rate dislodgeable after application and 16% daily dissipation (predicted) for squash treated by groundboom from the California test site,
- 20% of the application rate dislodgeable after application and 3% daily dissipation (predicted) for apples treated by airblast from the Washington test site,
- 15% of the application rate dislodgeable after application and 4% daily dissipation (predicted) for grapes treated by airblast from the California test site

The DFR values from the apple study were used to estimate exposure to workers contacting treated pome fruits, stone fruits and tree nuts as the crop morphology, foliage and application equipment are similar (orchard crop with smooth foliage, treated by airblast). For cucurbits, fruiting vegetables, Brassica head and stem vegetables, and leafy vegetables, the DFR values from the squash study were used to estimate worker exposure since groundboom application equipment is used for all of these field crops. Hairy leaf crops, such as squash, tend to have the highest DFR values; as such, the squash DFR data were used for all crops applied by groundboom even though the leaf texture is not the same for all these crops. To estimate worker exposure to treated small vine climbing fruits (excluding fuzzy kiwifruit), the DFR values from the grape study were used since grape is the representative crop of this crop subgroup (trellis crop with smooth foliage, treated by airblast).

Exposure estimates were compared to the toxicological endpoint to obtain the MOE; the target MOE is 100. The exposure and risk estimates are presented in Table 3.4.2.2-1. The calculated MOEs are all above the target MOE of 100. The restricted entry interval (REI) of 12 hours is adequate to protect re-entry workers.

Table 3.4.2.2-1 Postapplication exposure and risk estimate for Cyclaniliprole 50SL Insecticide on the day of last application

Crop / Re-entry activity (with highest transfer coefficient)	DFR ($\mu g/cm^2$)[1]	Transfer coefficient (cm^2/h)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI
Pome fruit (CG 11-09) - Thinning	0.405	3000	0.121	8230	12 hours
Stone fruit (CG 12-09) - Thinning	0.448	3000	0.134	7440	
Tree nuts (CG 14-11) - Scouting	0.405	580	0.023	42600	
Leafy vegetables (CG 4-13) - Hand weeding (Bok choy)	0.278	4400	0.122	8170	
Brassica head and stem vegetables (CG 5-13) - Hand harvesting	0.278	5150	0.143	6980	
Fruiting vegetables (CG 8-09) - Handset irrigation	0.278	1750	0.049	20500	
Cucurbit vegetables (CG 9) - Handset irrigation	0.278	1750	0.049	20500	
Small fruit vine climbing, except fuzzy kiwifruit (CSG 13-07F) - Girdling, turning grapes	0.287	19300	0.553	1810	

DFR = dislodgeable foliar residue, TC = transfer coefficient, MOE = margin of exposure, REI = restricted entry interval, CG = crop group, CSG = crop subgroup

[1] Calculated using the DFR values from three chemical specific DFR studies in apples, squash and grapes

[2] Transfer coefficients obtained from ARTF

[3] Exposure = (DFR [$\mu g/cm^2$] × TC [cm^2/h] × Exposure Duration (8 hours for workers)/ (80 kg bw × 1000 µg/mg)

[4] Based on NOAEL = 1000 mg/kg bw/day, target MOE = 100

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

Given that fruits and berries can be treated with cyclaniliprole, there is potential for exposure from pick-your-own activities. However, the postapplication occupational risk assessment is protective of the risk associated with dermal exposure to this scenario. In addition, there is no acute dietary endpoint identified for the general population, including infants and children, thus acute dietary and aggregate risk assessments from these scenarios are not required.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to 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 plant and animal commodities is cyclaniliprole. The residue definitions for risk assessment are cyclaniliprole and metabolite NK-1375 in plant products, and cyclaniliprole and metabolite NSY-28 in animal commodities.

The data gathering/enforcement analytical method JSM0269 is valid for the quantitation of cyclaniliprole and NK-1375 residues in crop matrices. The data gathering/enforcement analytical method JSM0277 is valid for the quantitation of cyclaniliprole, NK-1375, NSY-27, NSY-28 and YT-1284 residues in animal matrices. The residues of cyclaniliprole and metabolite NK-1375 are stable in representative matrices from five crop categories (high water, high oil, high protein, high starch and high acid content) for up to 18 months when stored at -20°C. Therefore, cyclaniliprole and NK-1375 residues are considered stable in all frozen crop matrices and processed crop fractions for up to 18 months. The raw agricultural commodities of tomato, apple, plum and grape were processed. Cyclaniliprole and NK-1375 residues concentrated in the processed commodities dried prunes (3.7× and 3.6×, respectively). Adequate ruminant feeding studies were carried out to assess the anticipated residues in animal matrices resulting from the current uses. There are no poultry or swine feed items associated with the use of cyclaniliprole, and quantifiable residues are not expected to occur in poultry or swine matrices. Crop field trials conducted throughout Canada and the United States using end-use products containing cyclaniliprole at approved rates in or on representative crops of leafy vegetables (crop group 4-13), brassica head and stem vegetables (crop group 5-13), fruiting vegetables (crop group 8-09), cucurbit vegetables (crop group 9), pome fruit (crop group 11-09), stone fruit (crop group 12-09), small fruits vine climbing crop subgroup, except fuzzy kiwifruit (crop subgroup 13-07f) and tree nuts (crop group 14-11) are sufficient to support the proposed maximum residue limits.

3.5.2 Exposure From Drinking Water

3.5.2.1 Concentrations in Drinking Water

The residue definition for drinking water includes cyclaniliprole and the major (>10%) transformation product NK-1375. NK-1375 was a major transformation product detected in phototransformation studies on soil and in water; it did not appear to be subject to phototransformation on soil. NK-1375 was detected in terrestrial field dissipation studies. This transformation product was deemed to have the potential to be found in drinking water sources. Other major transformation products of cyclaniliprole (NSY-137, TJ-537, NU-536-1 and NU-

536-2) were detected in aqueous phototransformation studies only, but these compounds further transformed to form minor components and carbon dioxide. NSY-137, TJ-537, NU-536-1 and NU-536-2 are not expected to be formed in significant quantities in the environment.

Estimated environmental concentrations (EECs) of the combined residues of cyclaniliprole (cyclaniliprole and transformation product NK-1375) in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of the combined residues of cyclaniliprole in groundwater were calculated using the Pesticide Root Zone Model - Groundwater (PRZM-GW) to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PRZM-GW are average concentrations in the top 1 metre of the water table. EECs of the combined residues of cyclaniliprole in surface water were calculated using the Surface Water Concentration Calculator (SWCC) model, which simulates pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in a vulnerable drinking water source, a small reservoir.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EECs are expected to allow for future use expansion into other crops at this application rate. Table 3.5.2.1-1 lists the application information and main environmental fate characteristics used in the simulations. A number of initial application dates between April and September were modelled. The model was run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Table 3.5.2.1-2 below. Details of water modelling inputs and calculations are available upon request.

Table 3.5.2.1-1 Major groundwater and surface water model inputs for Level 1 assessment of cyclaniliprole residues (cyclaniliprole and transformation product, NK-1375) in drinking water sources

Type of Input	Parameter	Value
Application Information	Crop(s) to be treated	Various vegetable, tree nut and fruit crops
	Maximum allowable application rate per year (g a.i./ha)	**Ecoscenario** Orchard crops: 300 Vegetable crops: 240 **Drinking water** 300
	Maximum rate each application (g a.i./ha)	**Ecoscenario** Orchard crops: 80, 60 Vegetable crops: 60 **Drinking water** 80, 60
	Maximum number of applications per year	4
	Minimum interval between applications (days)	**Ecoscenario** Orchard crops: 7

Type of Input	Parameter	Value
		Vegetable crops: 5 **Drinking water** 5
	Method of application	Aerial, airblast
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	Stable for cyclaniliprole and NK-1375
	Phototransformation half-life in water at 52°N latitude at 25°C (days)	1.35 for cyclaniliprole 0.84 for NK-1375
	Adsorption K_{OC} (mL/g)	533 (20th percentile of 5 K_{oc} values for cyclaniliprole) 25119 (only value for NK-1375)
	Aerobic soil biotransformation half-life (days)	1154 (90th percentile confidence bound on mean of 5 half-lives adjusted to 25ºC for cyclaniliprole) Stable for NK-1375
	Aerobic aquatic biotransformation half-life at (days)	349 (longest of two half-lives adjusted to 25ºC for cyclaniliprole) Stable for NK-1375
	Anaerobic aquatic biotransformation half-life (days)	234 (longest of two half-lives adjusted to 25ºC for cyclaniliprole) Stable for NK-1375

Table 3.5.2.1-2 Level 1 estimated environmental concentrations (EEC) of the combined residue of cyclaniliprole and transformation product, NK-1375, in potential drinking water sources

Use pattern*	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
3 × 80 g a.i./ha + 1 × 60 g a.i./ha, at 5-day intervals[5]	79	79	16	2.9

[1] 90th percentile of daily average concentrations
[2] 90th percentile of 365 day moving average concentrations
[3] 90th percentile of the peak concentrations from each year
[4] 90th percentile of yearly average concentrations
* The use pattern modelled covers the proposed uses on vegetable, tree nut and fruit crops

3.5.3 Dietary Risk Assessment

The chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™).

3.5.3.1 Chronic Dietary Risk Exposure Results and Characterization

The following criteria were applied to the basic chronic analysis for cyclaniliprole: 100% crop treated, default processing factors, and residues of cyclaniliprole in crops and animal commodities at MRL values. The basic chronic dietary exposure from all supported cyclaniliprole food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 5% of the acceptable daily intake (ADI). Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to cyclaniliprole from food and drinking water is 2.6% (0.0079 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1 – 2 years old at 5.0% (0.015 mg/kg bw/day) of the ADI.

3.5.3.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore, an acute dietary risk assessment was not required.

3.5.4 Aggregate Exposure and Risk

The aggregate risk for cyclaniliprole consists of exposure from food and drinking water sources only; there are no residential uses.

3.5.5 Maximum Residue Limits

Table 3.5.5.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Crop Group 4-13 (Leafy vegetables)	15
Crop Group 5-13 (Brassica head and stem vegetable group); Crop Group 12-09 (Stone fruits)	1
Crop Subgroup 13-07F (Small fruits vine climbing, except fuzzy kiwifruit)	0.8
Crop Group 11-09 (Pome fruits)	0.3
Crop Group 8-09 (Fruiting vegetables)	0.2
Crop Group 9 (Cucurbit vegetables)	0.15
Crop Group 14-11 (Tree nuts)	0.03
Meat byproducts and fat of cattle, goats, horses and sheep; milk	0.015
Meat of cattle, goats, horses and sheep	0.01

MRLs are proposed for each commodity included in the listed crop groupings in accordance with the Residue Chemistry Crop Groups webpage in the Pesticides and Pest Management portion of the Canada.ca website.

For additional information on Maximum Residue Limits (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 methodologies, field trial data, and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 6 and 7.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Cyclaniliprole is effectively stable to hydrolysis; therefore, hydrolysis is not expected to be an important route of dissipation of cyclaniliprole in the environment. Phototransformation on soil and near the surface of waterbodies may contribute to the dissipation of cyclaniliprole. The phototransformation half-life for cyclaniliprole was 25.8 days (based on a 12-hour light/dark cycle) on soil and 1.2 to 1.4 days (corrected for summer sunlight at 40°N latitude) in purified water and natural water, respectively. NK-1375 was a major (>10%) phototransformation product on soil; it did not appear to be subject to phototransformation. In water, cyclaniliprole was photodegraded to major transformation products NK-1375, NSY-137, TJ-537 and NU-536-1, NU-536-2. Further transformation occurred to form minor components, including NSY-28, and carbon dioxide. Volatilization of cyclaniliprole from water or moist soils is not expected.

Biotransformation of cyclaniliprole occurs slowly in the terrestrial and aquatic environment. In laboratory studies, half-lives of cyclaniliprole in soil ranged from 610 to 1728 days under both aerobic and anaerobic conditions. Minor (<10%) transformation products were measured in laboratory studies on soil: NSY-27 and YT-1284 (aerobic conditions only), an unidentified transformation product (anaerobic conditions only) and carbon dioxide. In water-sediment systems, total system half-lives for cyclaniliprole ranged from 495 to 854 days under both aerobic and anaerobic conditions. Minor transformation products NSY-28 (aerobic conditions only), unidentified 'Metabolite A' (anaerobic conditions only) and carbon dioxide were detected. Cyclaniliprole was associated with both the water and sediment phases in water-sediment systems.

Consistent with results of laboratory studies, cyclaniliprole dissipates slowly under terrestrial field conditions (representative field DT_{50} of 381 to 1247 days). Cyclaniliprole has the potential to accumulate in soil and carry over to the next growing season. Levels of cyclaniliprole remaining in the total soil column at the beginning of the next growing season were 24.8-91% of initial measured concentrations; residues remaining at the end of the study were 26.6-61.2% of initial measured levels. The phototransformation product, NK-1375, was a minor transformation product detected under field conditions, reaching maximum concentrations of 3.3-7.7% of initial measured parent concentrations within the first 30 days after application of cyclaniliprole, and subsequently declining at all sites.

The linear adsorption coefficient, K_d, and associated K_{oc} values for cyclaniliprole indicate that it is expected to have low to moderate mobility in a variety of soil types. Correlations were observed between the linear adsorption coefficient K_d and percent organic carbon and cation exchange capacity. Under terrestrial field conditions, cyclaniliprole leached beyond 30 cm at two of four test sites; as far down as a metre at one test site. Transformation product NK-1375 is expected to be immobile in soil based on its adsorption coefficient. In terrestrial field dissipation studies, NK-1375 was not detected below the 0-7.6 cm soil layer. Overall, taking into consideration results of laboratory studies, assessments using groundwater ubiquity scores (GUS) and criteria of Cohen et al. (1984), terrestrial field dissipation studies and conservative water modelling, cyclaniliprole is expected to leach to groundwater, however the major transformation product NK-1375 is not expected to leach.

Cyclaniliprole has low potential to bioaccumulate based on its octanol-water partitioning coefficient (log K_{ow}) value. A bioconcentration study in fish indicates that cyclaniliprole does not accumulate to a large degree in fish. The time for 95% depuration is estimated to be between 96 and 120 days.

Cyclaniliprole is not systemic but it has translaminar movement in plants. As such, cyclaniliprole applied by foliar spray is expected to mostly remain near leaves and not translocate throughout the plant.

The transformation products of cyclaniliprole detected in laboratory and field dissipation studies are summarized in Table 8 (Appendix I). The fate and behaviour of cyclaniliprole and its transformation products in the environment is summarized in Appendix I, Table 9.

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 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 (for example, 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 for most species, 0.4 for acute risk to pollinators, and 2 for glass plate studies using the standard beneficial arthropod test species, *Typhlodromus pyri* and *Aphidius rhopalosiphi*). 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 for cyclaniliprole was conducted for terrestrial organisms. For acute toxicity studies, uncertainty factors of 1/2 and 1/10 the EC_{50} (LC_{50}) are typically used in modifying the toxicity values for terrestrial invertebrates, birds and mammals when calculating risk quotients. No uncertainty factors are applied to chronic NOEC endpoints. A summary of terrestrial toxicity data for cyclaniliprole, its transformation product NK-1375 and the formulation Cyclaniliprole 50SL Insecticide is presented in Tables 10 and 11 (Appendix I). The screening level risk assessment for cyclaniliprole is presented in Appendix I, Table 12 for terrestrial organisms other than birds and mammals, and Appendix I, Table 13 for birds and mammals.

Earthworms: Cyclaniliprole and the end-use product Cyclaniliprole 50SL Insecticide were not toxic to earthworms based on acute and chronic exposure. The risk quotients for earthworms resulting from acute and chronic exposure to cyclaniliprole do not exceed the level of concern at the screening level. The risk quotient for earthworms resulting from acute exposure to the end-use product Cyclaniliprole 50SL Insecticide do not exceed the level of concern at the screening level. The use of cyclaniliprole is expected to pose a negligible acute risk to earthworms.

Other soil-dwelling invertebrates: Chronic exposure to cyclaniliprole in soil can affect the survival and reproduction of the Collembola, *Folsomia candida*. After 28 days, statistically significant effects on survival were observed at a concentration of 10 mg a.i./kg dry soil, whereas reproduction of Collembola was significantly reduced at concentrations of 5 mg a.i./kg dry soil and higher. Exposure to cyclaniliprole in soil for 14 days at a concentration of 1000 mg a.i./kg dry soil resulted in a 15% reduction in the reproduction of the predatory soil mite, *Hypoaspis aculeifer*. Using NOECs for reproduction in the calculations, the risk quotients for the reproduction of Collembola (*Folsomia candida*) and the predatory soil mite (*Hypoaspis aculeifer*) resulting from exposure to cyclaniliprole do not exceed the level of concern at the screening level. The use of cyclaniliprole is expected to pose a negligible risk to the reproduction of the soil-dwelling invertebrates Collembola and *H. aculeifer*.

Bees: Cyclaniliprole and Cyclaniliprole 50SL Insecticide were toxic to adult bees on an acute oral and contact basis, with the end-use product being more toxic than the TGAI. Chronic exposure to Cyclaniliprole 50SL Insecticide affected the survival of adult bees at doses of 0.05 µg a.i./bee/day and above. Cyclaniliprole was toxic to larval bees following single and repeated oral exposures above 0.0649 µg a.i./larva/day and 0.16 µg a.i./larva/day, respectively. In addition, bees experienced sublethal effects including apathy and problems with coordination in both the oral and contact exposure studies, which generally subsided by study termination in the oral exposure studies. Risk quotients were not exceeded for contact exposure to adult bees, and no risk was identified from the contact foliage residue study. However, risk quotients for adult and larval bees exceeded the level of concern at the screening (Tier I) level for oral exposure. Considering available relevant residue data, risk quotients for adult bees were exceeded for the refined screening level for oral exposure during early and mid-bloom. The risk to bees was further characterized using a weight-of-evidence approach considering the proposed uses of cyclaniliprole on crops and their attractiveness to bees, the fate and behaviour of cyclaniliprole in plants, as well as results from higher tier (semi-field and field) studies on bee colonies.

The proposed uses of cyclaniliprole on pome fruits and stone fruits are expected to result in exposure to bees, because of the attractiveness of these crops to bees. Although cucurbit vegetables are attractive to pollinators, particularly non-*Apis* species, flowers close in the afternoon and, therefore, pollen and nectar will not be contaminated with residues when spraying occurs in the evening after flowers close.

Cyclaniliprole has translaminar movement in plants and mostly remains near leaves once applied by foliar spray. As such, its use is not expected to result in oral exposure to bees through pollen and nectar when applied before or after bloom, or when flowers are closed.

Semi-field (Tier II) studies

Four studies were conducted under semi-field conditions to assess the potential effects to honey bee colonies following foliar application of the end-use product Cyclaniliprole 50SL Insecticide to blooming *Phacelia* crops. Application timing varied, but in all cases, bees were not present at the time of spraying. Bees were exposed for periods of 7 to 9 days, and then moved to another location (grassland) for continued monitoring. Hives were typically observed for mortality, foraging activity, behavioural abnormalities, colony strength, bee brood development, brood termination rate, brood index, and brood compensation index. All of the studies were conducted at application rates lower than the proposed rate, and in some cases, there was poor control hive development. In addition, rain or poor weather in two of the studies may have resulted in lower exposure/foraging. Control colonies were consistently part of the study design, and in some studies, fenoxycarb (an insect growth regulator expected to exert toxic effects on larvae) was used as a reference control. Residues were collected in many cases (3 out of 4 studies) in order to establish exposure to the colonies, and control contamination was evident in two of these studies. The overall findings from the semi-field studies are the following:

- Application in the morning at 80 g a.i./ha may result in adverse effects on honey bee colonies.
- Application during bloom in the evening (after bee activity) at up to 53 g a.i./ha does not appear to result in significant colony effects.
- There is a possible trend of short-term transient mortality for 1 day following application.

Field (Tier III) studies

Four studies were conducted under field conditions to assess the potential effects to honey bee colonies following foliar application of the end-use product Cyclaniliprole 50SL Insecticide. Three field studies were on *Phacelia* and one study was on canola. Application timing varied, but in most cases, bees were not present at the time of spraying. Bees were exposed for periods of 8 to 21 days, and then moved to another location for continued monitoring. Hives were typically observed for mortality, foraging activity, behavioural abnormalities, colony strength, bee brood development, brood termination rate, brood index, and brood compensation index. All of the studies were conducted at application rates lower than the proposed rate. Control colonies were consistently part of the study design, and in some cases control hives had poor colony development/high mortality. Residues were collected in many cases to establish exposure to the colonies, and control contamination was evident in one out of the four studies. The overall findings from the field studies are the following:

- Application during bloom in the evening (after bee activity) at up to 2 × 40 g a.i./ha may result in short-term mortality and decreased foraging.
- Application during bloom when bees are foraging at 40 g a.i./ha may result in short-term mortality.
- Application during bloom in the evening (after bee activity) at up to 2 × 60 g a.i./ha (on canola) may result in mortality and decreased colony strength.

Overall conclusions about potential risks to bees

Mitigation is required on the Cyclaniliprole 50SL Insecticide label in order to reduce exposure to bees from foraging on contaminated pollen and nectar. Applications are restricted on bee attractive crops during bloom.

Consideration of Mitigation

- Risk was identified from the Tier I risk assessment for oral exposure for adults and brood.
- Risk was identified from the Tier I refined assessment for early- and mid-bloom for adult bees.
- There were potential short-term effects from applications at 40 g a.i./ha, which is half of the proposed maximum rate of 80 g a.i./ha on orchard and berry crops. There were also potential effects on mortality and colony strength from applications at 60 g a.i./ha, which is three quarters of the proposed maximum orchard and berry rates (but equivalent to the maximum proposed rate for vegetable crops). Given the above, it is proposed to restrict applications during bloom on bee attractive crops.
- Cyclaniliprole has translaminar movement with little expected systemic movement into pollen and/or nectar from application onto leaves and/or stems. Therefore, pre-bloom and post-bloom applications are permitted on all crops. Application to closed flowers is also expected to result in limited residues in pollen and/or nectar.
- Mitigation (i.e. do not apply during bloom) is required for crops with high pollinator exposure, including stone fruit and pome fruit, or when managed bees are used for pollination services.
- Mitigation (i.e. application in the evening) is required for cucurbit crops since cucurbit flowers close in the afternoon and application to closed flowers is expected to result in limited residues in pollen and/or nectar. Application only in the evening after flowers have closed will reduce exposure for *Apis* and non-*Apis* species such as the squash bee.
- Mitigation (i.e. application in the evening) is required for all other crops.

Beneficial arthropods: Acute exposure of the predatory mite, *Typhlodromus pyri*, and the parasitoid wasp, *Aphidius rhopalosiphi*, to a formulation of cyclaniliprole on glass plates resulted in significant effects in reproduction and survival. The risk quotients for the *A. rhopalosiphi*, but not *T. pyri*, exceeded the level of concern when using endpoints from toxicity on glass plates (screening level) (Table 12, Appendix I). The risks to predatory and parasitic arthropods was further characterized using results from higher tier (extended laboratory/aged residue) toxicity studies with *A. rhopalosiphi* and other terrestrial arthropod species.

Extended laboratory/aged residue studies

In an extended laboratory/aged residue study, exposure to fresh residues of Cyclaniliprole 50SL Insecticide on plant leaves at approximately 4 g a.i./ha affected the survival and fecundity of *A. rhopalosiphi* on the day of application. The survival of *A. rhopalosiphi* was affected following exposure to residues of Cyclaniliprole 50SL Insecticide aged up to 14 days, while effects on fecundity were observed following exposure to residues aged for up to 28 days following application. In extended laboratory/aged residue studies conducted with other arthropods, exposure to fresh residues of Cyclaniliprole 50SL Insecticide on plant leaves at approximately 28 g a.i./ha affected the pre-imaginal survival, but not the fecundity of the ladybird beetle, *Coccinella septempunctata*. Exposure of the ladybird beetle to dry residues aged for 28 days or more after application did not result in toxicity up to the highest rate tested of 80 g a.i./ha. Fresh residues of Cyclaniliprole 50SL Insecticide on soil at approximately 80 g a.i./ha affected the survival of the rove beetle, *Aleochara bilineata*, and fecundity was reduced by 31%, but dry residues of cyclaniliprole were no longer toxic within 14 days following application up to the highest tested rate of 80 g a.i./ha. The highest rate tested in these extended laboratory/aged residue studies (80 g a.i./ha) was less than the maximum cumulative rates of application proposed for use on crops in Canada.

Based on exposure of *A. rhopalosiphi* to residues of Cyclaniliprole 50SL Insecticide on bean plants on the day of application (0 days after treatment, DAT), the risk quotients for survival and reproduction exceeded the level of concern for in-field exposure (RQs = 32-34) and off-field exposure from early season airblast application (RQs = 3.0-3.1) (Appendix I, Table 14).

For in-field exposure of *A. rhopalosiphi* to residues aged for 14 days, risk quotients exceed the level of concern for mortality and reproductive effects (RQs = 5.8-11). Considering residues aged for 28 days, the risk quotient from in-field exposure exceed the level of concern for reproductive effects (RQ = 2.9), and may exceed the level of concern for survival (RQ <1.7). Based on results for residues aged 56 days, the risk quotients for in-field exposure may exceed the level of concern for survival and reproductive effects (RQs <1.7). There is uncertainty related to the potential for effects on survival following in-field exposure to Cyclaniliprole 50SL Insecticide residues aged for 28 to 56 days and on reproduction following in-field exposure to residues aged for 56 days because the rates tested in the studies were lower than the maximum cumulative rates proposed for cyclaniliprole in Canada.

For off-field exposure of *A. rhopalosiphi* to residues of Cyclaniliprole 50SL Insecticide aged for 14 to 56 days, risk quotients do not exceed the level of concern for survival (Appendix I, Table 14). The risk quotient for reproductive effects exceeds the level of concern for residues aged 14 days (RQ = 1.0), but does not exceed the level of concern for residues aged longer than 14 days.

Semi-field or field toxicity studies were not available to further characterize the risks to *A. rhopalosiphi*, or to assess the potential for recovery following effects. Recolonisation is expected based on the lack of off-field effects on survival and reproduction following exposure to residues aged longer than 14 days.

Extended laboratory/aged residue studies using other foliage and soil dwelling arthropod species were available to characterize the risk of Cyclaniliprole 50SL Insecticide to non-target arthropods. Using mortality endpoints (LR_{50}s) from extended laboratory/aged residue studies on the ladybird beetle, *Coccinella septempunctata*, and the rove beetle, *Aleochara bilineata*, risk quotients for both species exceed the level of concern for in-field exposure immediately following application (RQ = 2.8-5.0), and may exceed the level of concern for in-field exposure to residues aged for up to 56 days after application to stone fruits (RQs<1.7 to <3.0) (Appendix I, Table 14).

Using reproduction endpoints (ER_{50}s) from the same extended laboratory/aged residue studies, risk quotients for the ladybird beetle and the rove beetle may exceed the level of concern for in-field exposure to residues immediately following application and to residues aged for up to 56 days following application to stone fruits (RQs<1.7 to <5.1) (Appendix I, Table 14).

There is uncertainty as to whether risk quotients for survival following in-field exposure to aged residues of Cyclaniliprole 50SL Insecticide, and those for reproductive effects following in-field exposure to residues and aged residues of Cyclaniliprole 50SL Insecticide exceed the level of concern because the rates tested in the studies were lower than the maximum cumulative rates proposed for cyclaniliprole in Canada. Semi-field or field toxicity studies were not available to assess the potential for recovery following effects.

The risk quotients for off-field exposure of the ladybird beetle and the rove beetle to residues on the day of application and to aged residues of Cyclaniliprole 50SL Insecticide did not exceed the level of concern for survival or reproduction (Appendix I, Table 14). Thus, recolonisation is expected.

Overall conclusions about potential risks to beneficial arthropods

It is possible that uses of Cyclaniliprole 50SL Insecticide could result in in-field and off-field effects on *Aphidius rhopalosiphi*, and in-field effects on *Coccinella septempunctata* and *Aleochara bilineata*. Studies conducted with rates of application corresponding to the maximum cumulative rates proposed for use were not available, nor were semi-field or field tests conducted to further characterize the risks. To minimize exposure and reduce potential risks to beneficial arthropods, a precautionary statement is required on the label for the end-use product Cyclaniliprole 50SL Insecticide.

Birds: Cyclaniliprole exhibited low acute toxicity to birds via oral and dietary routes. Chronic studies with cyclaniliprole indicated effects on the reproduction of bobwhite quail at 300 and 1000 mg a.i./kg diet. These were effects on eggshell thickness, viable embryos of eggs set, live 3-week embryos as a proportion of those viable, normal hatchlings of viable embryos and of live 3-week embryos, 14-day survivors of eggs laid, and chick bodyweights at 14 days. The risk quotients for birds resulting from acute oral exposure to cyclaniliprole did not exceed the level of concern at the screening level. The screening level risk quotients for birds resulting from reproductive exposure slightly exceeded the level of concern for small- and medium-sized insectivores (RQs of 1.6 and 1.3, respectively; Appendix I, Table 13). The risks to birds was further characterized considering other feeding guilds, on-field and off-field exposures, maximum and mean residue levels as well as a calculating risk quotients using the reproductive Lowest Observable Effects Level (LOEL) to bracket the description of risk.

Looking at multiple feeding guilds, risk quotients still only slightly exceeded the level of concern for small- and medium-sized insectivorous birds when considering maximum residue levels on the field (RQs of 1.6 and 1.3, respectively; Appendix I, Table 15). Assuming that food items all contain maximum residue levels is conservative; levels will likely vary. Risk quotients calculated using mean residues of cyclaniliprole only slightly exceeded the level of concern for small insectivores exposed on the field (RQ of 1.1; Appendix I, Table 16).

Risks from off-field exposure were investigated assuming 74% drift from early season airblast applications. Risk quotients for off-field exposure only slightly exceeded the level of concern for small insectivores consuming food items with maximum residue levels (RQ = 1.2; Appendix I, Table 15). No risk quotient for any feeding guild exceeded the level of concern when considering mean residues off-field (Appendix I, Table 16). It should be noted that the other methods of application proposed for use of cyclaniliprole involve less spray drift than early season airblast application (late season airblast: 59% drift; aerial application: 26% for fine droplet size; field sprayer application: 11% for fine droplet size). Thus, the off-site risks from these methods of application are expected to be less than those from early season airblast application.

Using a LOEL for reproductive effects of 25.7 mg a.i./kg bw/day in the calculations instead of a NOEL of 8.8 mg a.i./kg bw/day, no risk quotients exceeded the level of concern (Appendix I, Table 17).

The few risk quotients above the level of concern were all close to 1.0 and involved only a small number of feeding guilds (small- and medium-sized insectivorous birds). Levels on food items are likely variable and thus assuming that 100% of food items contain maximum residue levels is conservative. No risk quotient exceeded the level of concern when considering mean residues off-field. No risk quotient exceeded the level of concern when using a LOEL for reproduction in the risk calculations. Based on these results, the concern for reproductive risks of cyclaniliprole to birds is low.

Mammals: Cyclaniliprole and the formulation Cyclaniliprole 50SL Insecticide were not toxic to small mammals based on acute oral and two-generation reproduction studies. The risk quotients for mammals resulting from acute and reproduction exposure to cyclaniliprole did not exceed the level of concern at the screening level. Cyclaniliprole is expected to pose negligible risk to mammals.

The results of an acute oral toxicity study with the transformation product NK-1375 indicate that the transformation product is not toxic toxic to mammals, similar to the parent cyclaniliprole. Considering that the risk quotients for acute exposure to cyclaniliprole are below the level of concern, the transformation product NK-1375 is expected to pose a negligible risk to mammals. Risk quotients using endpoints for the transformation product have not been generated.

Vascular plants: Cyclaniliprole 50SL Insecticide did not significantly affect seedling emergence or vegetative vigour in vascular plant species at rates up to 1000 g a.i./ha and the corresponding risk quotients do not exceed the level of concern at the screening level. Cyclaniliprole is expected to pose a negligible risk to terrestrial vascular plants.

4.2.2 Risks to Aquatic Organisms

A risk assessment for cyclaniliprole, the transformation products NK-1375, NU-536 and TJ-537, and the formulation Cyclaniliprole 50SL Insecticide was conducted for freshwater and marine aquatic organisms based on available toxicity data. A summary of aquatic toxicity data is presented in Appendix I, Table 18.

For acute toxicity studies, uncertainty factors of 1/2 and 1/10 the EC_{50} (LC_{50}) are typically used for aquatic plants and invertebrates, and fish species, respectively, when calculating risk quotients (RQs). No uncertainty factors are applied to chronic NOEC endpoints. For groups where the level of concern (LOC) is exceeded (thus, if $RQ \geq 1$), a refined Tier 1 assessment is conducted to determine risk resulting from spray drift and runoff separately. Risk quotients for cyclaniliprole and its transformation products were calculated based on the highest maximum seasonal application rate for all uses. The screening level risk quotients for cyclaniliprole, the formulation Cyclaniliprole 50SL Insecticide and the cyclaniliprole transformation products are summarized in Tables 19, 20 and 21, respectively, in Appendix I. The risk quotients for the Tier 1 assessment of cyclaniliprole and Cyclaniliprole 50SL Insecticide are presented in Appendix I, Table 22 (spray drift only) and Appendix I, Table 23 (runoff only).

Invertebrates: Cyclaniliprole and the end-use product Cyclaniliprole 50SL Insecticide were toxic to *Daphnia magna* at low concentrations on an acute basis. Chronic exposure to cyclaniliprole at 0.015 mg/L affected the reproduction of *D. magna*. In an acute toxicity test involving water only, 45% of midges, *Chironomus riparius*, were immobilized following exposure to cyclaniliprole at 0.0533 mg/L. In a chronic spiked sediment toxicity test cyclaniliprole did not appear to have a significant impact on the development rate or sex ratio profile of the midge at a sediment concentration of 0.061 mg a.i./kg. In laboratory tests with marine invertebrates, cyclaniliprole was not acutely toxic to the mysid shrimp, *Americamysis bahia*, up to the limit of solubility in water under the conditions of the test. Cyclaniliprole was toxic to the Eastern oyster, *Crassostrea virginica*, at low concentrations on an acute basis.

The screening level risk quotients for exposure to cyclaniliprole or its end-use product Cyclaniliprole 50SL Insecticide at the proposed application rates for stone fruits exceeded the level of concern for the freshwater invertebrates *Daphnia magna* and *Chironomus riparius*, and the marine/estuarine mollusk, *Crassostrea virginica*.

The refined risk quotients indicate that the level of concern from cyclaniliprole exposure through spray drift is exceeded for *D. magna* (chronic exposure), *C. riparius* (acute exposure) and *C. virginica* (acute exposure) (Appendix I, Table 22). Spray buffer zones will be required to mitigate potential effects of cyclaniliprole drift on aquatic organisms in adjacent freshwater and estuarine/marine habitats. The spray buffer zones for cyclaniliprole will be rate-specific for the product labels and will range from 1 to 3 metres.

Risk quotients for freshwater and marine/estuarine invertebrates from exposure to cyclaniliprole through runoff did not exceed the level of concern (Appendix I, Table 23).

Phototransformation products NK-1375 and TJ-537 were not toxic to *D. magna* on an acute basis up to the limit of water solubility of the compounds under the conditions of the tests. NU-536 was not toxic to *D. magna* up to the highest concentration tested of 24.4 mg/L. The risk quotient for acute exposure of *D. magna* to transformation products NU-536 and TJ-537 did not exceed the level of concern at the screening level (Appendix I, Table 21). The risk quotient for acute exposure of *D. magna* to transformation product NK-1375 was less than 1.3. This value was derived using an EEC in a 80-cm deep body of water, and an endpoint of greater than 0.0272 mg a.i./L (96-hour LC_{50} > 0.0543/2). Based on the low risk quotient and because 0% immobilization was observed up to the highest concentration tested which approached the limit of solubility of cyclaniliprole in water under the conditions of the test, a risk to *D. magna* from the transformation product NK-1375 is not expected.

Fish: Cyclaniliprole was not toxic to freshwater or marine fish. No mortalities were observed in any acute or early life stage toxicity study up to the highest concentrations tested which approached the limit of solubility of cyclaniliprole in water under the conditions of the tests. Acute exposure to high concentrations of the end-use product Cyclaniliprole 50SL Insecticide affected the survival of rainbow trout.

The risk quotients for freshwater fish resulting from acute and early-life stage exposure to cyclaniliprole did not exceed the level of concern at the screening level (Appendix I, Table 19). The risk quotient for freshwater fish resulting from acute exposure to the end-use product Cyclaniliprole 50SL Insecticide did not exceed the level of concern at the screening level.

The risk quotient for marine fish resulting from acute exposure to cyclaniliprole was less than 2.3. This value was derived using an EEC in an 80-cm deep body of water, and an endpoint of greater than 0.016 mg a.i./L (96-hour LC_{50} > 0.16/10) for the sheepshead minnow. Based on the relatively low risk quotient and because 0% mortality was observed up to the limit of solubility of cyclaniliprole in water under the conditions of the test, a risk to marine or estuarine fish is not expected.

The use of cyclaniliprole is expected to pose a negligible risk to fish.

Amphibians: The risk for amphibians was characterized at the screening level by comparing EECs in 15 cm water depth with amphibian toxicity endpoints for cyclaniliprole. The risk quotient for amphibians resulting from acute exposure to cyclaniliprole was less than 3.1 (Appendix I, Table 19). This value was derived using an EEC in a 15-cm deep body of water, and an endpoint of greater than 0.063 mg a.i./L (96-hour LC_{50} > 0.63/10) for fish. Based on the relatively low risk quotient and because 0% mortality was observed up to the limit of solubility of cyclaniliprole in water under the conditions of the test with fish, a risk to amphibians from acute exposure is not expected. Using an endpoint from an early-life stage study with fish, the risk quotient for amphibians resulting from a stage-specific exposure to cyclaniliprole did not exceed the level of concern at the screening level.The risk quotient for amphibians resulting from acute exposure to the end-use product Cyclaniliprole 50SL Insecticide did not exceed the level of concern at the screening level (Appendix I, Table 20).

The use of cyclaniliprole is expected to pose a negligible risk to amphibians.

Algae: Cyclaniliprole was not toxic to freshwater or marine algae up to the highest concentrations tested which approached the limit of solubility of cyclaniliprole in water under the conditions of the tests. Exposure to high concentrations of the formulation Cyclaniliprole 50SL Insecticide inhibited the cell density and yield of green algae. The risk quotients for freshwater and marine algae resulting from acute exposure to cyclaniliprole did not exceed the level of concern at the screening level (Appendix I, Table 19). The risk quotient for freshwater algae resulting from acute exposure to the formulation Cyclaniliprole 50SL Insecticide did not exceed the level of concern at the screening level. The use of cyclaniliprole is expected to pose a negligible risk to freshwater or marine algae.

Aquatic vascular plants: Cyclaniliprole was not toxic to aquatic vascular plants up to the highest concentration tested which approached the limit of solubility of cyclaniliprole in water under the conditions of the tests. The risk quotients for aquatic vascular plants resulting from exposure to cyclaniliprole did not exceed the level of concern at the screening level (Appendix I, Table 19). The use of cyclaniliprole is expected to pose a negligible risk to aquatic vascular plants.

5.0 Value

5.1 Consideration of Benefits

Cyclaniliprole 50SL Insecticide is a new tool for the control of several insect pests on labelled vegetable, tree nut and fruit crops. Two other Group 28 active ingredients, chlorantraniliprole and cyantraniliprole, are registered for use in Canada. Products containing these active ingredients are registered for most of the uses of Cyclaniliprole 50SL Insecticide. However, Cyclaniliprole 50SL Insecticide is the first insecticide proposed for registration in Canada to control walnut husk fly on stone fruits, and omnivorous leafroller on stone fruits and small fruits (vine climbing) other than grapes.

Cyclaniliprole represents a new mode of action for use on small fruits (vine climbing) against spotted wing drosophila, an invasive pest which is difficult to control. It is also a new mode of action against walnut husk fly on tree nuts, whiteflies on labelled vegetable crops and omnivorous leafroller on grapes. Therefore, cyclaniliprole will be useful for resistance management on these crop-pest combinations.

5.2 Effectiveness Against Pests

Four laboratory trials, 84 field trials conducted on a wide variety of crops in the United States and Canada, and rationales for extrapolations were provided to support the use of Cyclaniliprole 50SL Insecticide to control or suppress various insect pests on labelled vegetable, fruit and tree nut crops (see Appendix I, Table 25). Trials supported the majority of label claims including important pests on fruit crops, such as codling moth and grape berry moth, and on vegetable crops, such as cabbage looper and western flower thrips. Extrapolations based on similar life cycle and feeding damage were used to support three caterpillar species on the listed crops. Extrapolation was also used to support pest claims between crop groups when required.

Cyclaniliprole 50SL Insecticide controlled all of the listed pests, except a claim of suppression was supported for apple maggot, plum curculio, omnivorous leafroller, onion thrips, western flower thrips and whiteflies. An application rate range was accepted for almost all crop-pest combinations. In these cases, the label recommends using the higher rate under high pest pressure. For codling moth on tree nuts, and whiteflies, thrips and dipteran leafminers on the listed vegetable crops, only the higher application rates are accepted.

5.3 Non-Safety Adverse Effects

In the 84 field trials, conducted on a wide variety of vegetable, fruit and tree nut crops, non-safety adverse effects (i.e. phytotoxicity) were not reported in the treated crops.

5.4 Supported Uses

The reviewed value information supported the use of Cyclaniliprole 50SL Insecticide as a foliar spray against a variety of insect pests on labelled vegetable, fruit and tree nut crops. Application rates are 1.2-1.6 L/ha for the fruit and tree nut crops, and 0.8-1.2 L/ha for the vegetable crops. It is applied to all listed crops by ground application and to the vegetable crops by aerial application. The higher rate is to be used when pest pressure is high. See Appendix I, Table 25 for details.

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), bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, cyclaniliprole 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 following conclusions:

- Cyclaniliprole does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix I, Table 24 for comparison with Track 1 criteria.
- NK-1375 is a major product of phototransformation on soil and in water. It is not expected to persist in soil based on results of terrestrial field dissipation studies.
- NSY-137, NU-536-1, NU-536-2 and TJ-537 are major products of aqueous phototransformation only. They were further phototransformed to carbon dioxide and minor components in laboratory studies. They are therefore not expected to be persistent. NSY-137, NU-536-1, NU-536-2 and TJ-537 are not expected to be formed in significant quantities in the environment.

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.*[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: DIR99-03; and DIR2006-02,[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 following conclusions:

- Technical grade cyclaniliprole and the end-use product Cyclaniliprole 50SL Insecticide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*
- The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

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

6 *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.*

7 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.*

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for cyclaniliprole was adequate to define the majority of toxic effects that may result from exposure. Cyclaniliprole demonstrated a low overall level of toxicity based on the results of testing that was conducted at high doses, the majority of which was at or above the limit dose of testing. There was no evidence of carcinogenicity in rats or mice after longer-term dosing. There was no evidence of toxicity to the young or developing animal in the reproduction or developmental toxicity studies. Cyclaniliprole was not neurotoxic or genotoxic and was not considered to be an immunotoxicant. In short- and long-term studies on laboratory animals, the primary target was the liver, with marginally adverse effects observed in dogs only, and only at high dose levels. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which the effects occurred in animal tests.

Mixers, loaders, and applicators handling Cyclaniliprole 50SL Insecticide and workers entering treated areas are not expected to be exposed to levels of cyclaniliprole that will result in health risks of concern when the product is used according to label directions. The personal protective equipment on the product label is adequate to protect workers. Additionally, no health risks of concern were identified for the general public re-entering treated areas to perform pick-your-own activities.

The nature of the residues in plants (apple, lettuce, potato) and animals (poultry and goat) is adequately understood. The residue definition for enforcement is cyclaniliprole in plant and animal matrices. The use of cyclaniliprole on leafy vegetables (crop group 4-13), brassica head and stem vegetables (crop group 5-13), fruiting vegetables (crop group 8-09), cucurbit vegetables (crop group 9), pome fruit (crop group 11-09), stone fruit (crop group 12-09), small fruits vine climbing crop subgroup, except fuzzy kiwifruit (crop subgroup 13-07F) and tree nuts (crop group 14-11) does not constitute a health risk of concern for chronic dietary exposure (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 MRLs. The PMRA recommends that the following MRLs be specified for residues of cyclaniliprole.

Commodity	Recommended MRL (ppm)
Crop Group 4-13 (Leafy vegetables)	15
Crop Group 5-13 (Brassica head and stem vegetable group); Crop Group 12-09 (Stone fruits)	1
Crop Subgroup 13-07F (Small fruits vine climbing, except fuzzy kiwifruit)	0.8
Crop Group 11-09 (Pome fruits)	0.3
Crop Group 8-09 (Fruiting vegetables)	0.2
Crop Group 9 (Cucurbit vegetables)	0.15

Commodity	Recommended MRL (ppm)
Crop Group 14-11 (Tree nuts)	0.03
Meat byproducts and fat of cattle, goats, horses and sheep; milk	0.015
Meat of cattle, goats, horses and sheep	0.01

7.2 Environmental Risk

The use of Cyclaniliprole 50SL Insecticide containing the active ingredient cyclaniliprole at the proposed label rates does not pose a risk of concern to wild mammals, birds, fish and amphibians. It may, however, pose a risk to bees, beneficial predatory and parasitic arthropods, and freshwater and marine invertebrates. Risks to these organisms can be mitigated with label statements and spray buffer zones to protect sensitive terrestrial and aquatic habitats from spray drift. Risks to bees can also be mitigated by restricting application during the blooming period of crops that are highly attractive to pollinators such as pome fruits and stone fruits, or when managed bees are used for pollination services. Risks can be mitigated for bees (including squash bees) by limiting application to the evening for cucurbits when flowers are not open. Statements are required on the label for Cyclaniliprole 50SL Insecticide to inform users of the potential risks of leaching and carry-over of cyclaniliprole.

7.3 Value

Cyclaniliprole 50SL Insecticide provides growers with a new product for use against a variety of insect pests on labelled vegetable, tree nut and fruit crops. It can be applied to foliage by ground application to all listed crops and by aerial application to the vegetable crops. Other diamide products are registered for most of the uses of Cyclaniliprole 50SL Insecticide. However, it is the first insecticide proposed for registration in Canada to control walnut husk fly on stone fruits, and omnivorous leafroller on stone fruits and small fruits (vine climbing) other than grapes. Also, it represents a new mode of action for certain crop-pest combinations including spotted wing drosophila on small fruits (vine climbing). Therefore, cyclaniliprole will be useful for resistance management on these crop-pest combinations.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Technical Cyclaniliprole Insecticide and Cyclaniliprole 50SL Insecticide, containing the technical grade active ingredient cyclaniliprole, as a foliar insecticide to suppress or control various insect pests on various vegetable, tree nut and fruit crops.

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

List of Abbreviations

^{14}C	Carbon-14 radioactive isotope
♀	female
♂	male
°C	degrees Celsius
µg	microgram(s)
1/n	exponent for the Freundlich isotherm
aa	after application
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
ALP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
atm	atmosphere
ATPD	area treated per day
AUC	area under the curve
BAF	bioaccumulation factor
BBCH	Biologische Bundesanstalt, Bundessortenamt und Chemische Industrie
BCF	bioconcentration factor
ba	before application
bw	body weight
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CCA	colony condition assessment
CEPA	*Canadian Environmental Protection Act*
CG	crop group
cm	centimetre(s)
C_{max}	maximum concentration
CMC	carboxymethylcellulose
CSG	crop subgroup
d	day(s)
DAFA	days after first application
DAST	days after second treatment
DAT	days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model – Food Commodity Intake Database
DFOP	double first-order in parallel
DFR	dislodgeable foliar residue
dm	decimetre(s)
DT_{50}	dissipation time 50%
DT_{90}	dissipation time 90%
EC_{50}	effective concentration on 50% of the population
EDE	estimated dietary exposure
EEC	estimated environmental concentration

ER_{25}	effective rate for 25% of the population
ER_{50}	effective rate on 50% of the population
FIR	food ingestion rate
g	gram(s)
GAP	Good Agricultural Practice
GLP	Good Laboratory Practices
GI	gastrointestinal
GUS	groundwater ubiquity score
ha	hectare(s)
HAFT	highest average field trial
HDPE	high density polyethylene
HPLC-MS/MS	high-performance liquid chromatography with tandem mass spectrometryh
h	hour(s)
IMP	initial measured parent
IRAC	Insecticide Resistance Action Committee
IUPAC	International Union of Pure and Applied Chemistry
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
K_{FOC}	organic carbon normalized Freundlich adsorption coefficient
kg	kilogram(s)
km	kilometre(s)
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
kPa	kilopascal(s)
L	litre(s)
LAFT	lowest average field trial
LC_{50}	lethal concentration 50%
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEL	lowest observed effect level
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
LSC	liquid scintillation counting
m	metre(s)
M/L	mixer/loader
MAS	maximum average score
MBD	more balanced diet
mg	milligram(s)
MIS	maximum irritation score
mL	millilitre(s)
MOE	margin of exposure
mol	mole(s)
MRL	maximum residue limit
MW	molecular weight

n	number of field trials
nd	not detected
nm	nanometre(s)
N	North
N/A	not applicable
NAFTA	North American Free Trade Agreement
NOAED	no observed adverse effect dose
NOAEL	no observable adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NZW	New Zealand White
OECD	Organization for Economic Cooperation and Development
Pa	Pascal(s)
PBI	plant-back interval
PFC	plaque-forming colonies
pH	measure of the acidity or basicity of an aqueous solution
Ph	phenyl ring position radiolabel
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*Ka*	dissociation constant
PMRA	Pest Management Regulatory Agency
POD	point of departure
ppb	parts per billion
ppm	parts per million
PRZM-GW	Pesticide Root Zone Model - Groundwater
Pz	pyrazole radiolabel
REI	restricted entry interval
RQ	risk quotient
RT_{25}	Residual time needed to reduce the activity of the test substance and bring bee mortality down to 25%
SD	standard deviation
SFO	single first-order
SWCC	Surface Water Concentration Calculator
$t_{1/2}$	half-life
TC	transfer coefficient
TGAI	technical grade active ingredient
T_{max}	time to peak blood concentration
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
U.S. EPA	United States Environmental Protection Agency
UV	Ultraviolet
wt	weight

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference (PMRA #)
Soil	Not stated	Cyclaniliprole, NK-1375	HPLC-MS/MS	2 ppb	2398874
Water	Not stated	Cyclaniliprole, NK-1375, NSY-137, TJ-537, NU-536	HPLC-MS/MS	0.1 ppb	2398877
Plant	JSM0269	Cyclaniliprole, NK-1375	LC-MS/MS	0.01 ppm per analyte	2399090, 2399093, 2399099
Animal	JSM0277	Cyclaniliprole, NK-1375 NSY-27 NSY-28 YT-1284	LC-MS/MS	0.01 ppm per analyte	2398881, 2444435, 2444436

Table 2 Common Name of Cyclaniliprole Metabolites

Compound/Metabolite	Chemical Name
Cyclaniliprole	3-bromo-*N*-[2-bromo-4-chloro-6[[(1 cyclopropylethyl) amino]carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1*H*-pyrazole-5-carboxamide
NK-1375	3-bromo-2-[(2-bromo-4*H*- pyrazolo[1,5-*d*]pyrido[3,2-*b*]-[1,4]oxazin-4-ylidene)amino]-5-chloro-*N*-(1-cyclopropylethyl)benzamide
NSY-27	3-bromo-2-[3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamido]-5-chlorobenzoic acid
NSY-28	8-bromo-2-[3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazol-5-yl]-6-chloroquinazolin-4(3*H*)-one
YT-1284	3-bromo-*N*-(2-bromo-6-carbamoyl-4-chlorophenyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamide

Table 3 Toxicity Profile of the End-use Product Cyclaniliprole 50SL Insecticide Containing Cyclaniliprole

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study Type/ Animal/ PMRA #	Study Results
Oral toxicity (Acute toxic class) Sprague-Dawley Rat PMRA # 2399177	LD_{50} (♀) > 2000 mg/kg bw Low acute toxicity
Dermal toxicity Sprague-Dawley Rat PMRA # 2399178	LD_{50} > 2000 mg/kg bw Low acute toxicity
Inhalation toxicity (nose-only) Wistar Rat PMRA # 2399179	LC_{50} > 5.05 mg/L Low acute toxicity
Eye irritation NZW Rabbit PMRA # 2399181	MIS (unrinsed) = 10 MAS (unrinsed) = 1.56 MIS (rinsed) = 10.7 MAS (rinsed) = 1.56 Minimally irritating
Dermal irritation NZW Rabbit PMRA # 2399180	MAS = 0 MIS = 0 Non irritating
Dermal sensitization (Local Lymph Node Assay) CBA/J Mice PMRA # 2399182	Not a dermal sensitizer
Dermal Sensitization (Buehler test) Hartley Guinea Pigs PMRA # 2444534	Not a dermal sensitizer

Table 4 Toxicity Profile of Technical Cyclaniliprole

(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)

Study Type/ Animal/ PMRA #	Study Results
Toxicokinetics/ Metabolism Han Wistar Rat PMRA # 2398882	Rats received a single oral low (10 mg/kg bw) or high (400 mg/kg bw) dose of [^{14}C-Ph]-cyclaniliprole or [^{14}C-Pz]-cyclaniliprole via gavage (in 0.5% aqueous CMC) for investigation of excretion, biliary elimination (^{14}C-Ph label only), toxicokinetics, tissue distribution, or metabolism. Rats were also dosed with [^{14}C-Ph]-cyclaniliprole at 10 mg/kg bw/day for 14 days to investigate excretion, distribution or kinetics. Cyclaniliprole was poorly absorbed in rats. Only 11/9 % (♂/♀) of the administered dose (AD) was absorbed within 48 hours of administration of the low dose. At the high dose, absorption was 2/5% (♂/♀) of the AD within 48 hours of administration. Regardless of dose, the majority of the AD (85%) was eliminated within 48 hours, mostly via the feces. Urine accounted for less than 1% of the AD. As bile levels were approximately 3% of the AD at the low dose and 0.8 % of the AD at the high dose, most of the radioactivity found in feces represented unabsorbed compound. No radioactivity was detected in expired air. The excretion pattern was similar following repeat dosing. Following single dosing in rats, plasma concentration peaked and remained elevated after 24 hours, and reached a maximum between 24 and 120 hours, with ♂ peaking before ♀. Plasma levels were higher in ♂, with both peak concentration (Cmax) and area under the curve (AUC) being 35-75% or 50-75% higher, respectively. Levels of radioactivity at the high dose were higher than at the low dose, but did not increase linearly – a 40-fold increase in dose resulted in approximately 8-fold increases in AUC and C_{max}. There were no significant differences between the toxicokinetic profiles of the two radiolabels. Following repeat dosing, extensive accumulation of radioactivity occurred in plasma or whole blood. Terminal half-lives could not be calculated due to the fact that levels of radioactivity did not significantly decline in the post- dosing period (0-120 or 0-168 hours). In rats following single dosing, highest tissue concentrations were noted in plasma or whole blood, followed by liver, lungs, adrenals, fat, thyroid, ovaries or epididymides. Levels in red blood cells were below detection

Study Type/ Animal/ PMRA #	Study Results
	levels. Tissue concentrations were similar between ♂ and ♀. Overall, following a single dose, tissue accumulation was low after 168 hours (3% of AD at low dose, 1% at high dose). Following repeat dosing, 31% of the AD remained in tissues, resulting in tissue concentration increasing by 10-40 fold. Tissue concentration did not decrease significantly over time with the exception of GI tract content and liver. The majority of the AD was eliminated in rats via the feces (approximately 75-95%) and consisted of unchanged cyclaniliprole. The metabolites NSY-27, NSY-28, or YT-1284 were identified in bile or in urine, in each case accounting for less than 1% of the AD. Unchanged cyclaniliprole was not detected in urine or bile. NSY-28 was the major metabolite found in plasma, accounting for 91-96% of plasma radioactivity; unchanged cyclaniliprole accounted for 2-5%. NSY-28 was also the major metabolite in the kidney. Higher quantities of unchanged cyclaniliprole were found in liver or fat. NK-1375 was also found in the fat. The proposed metabolic pathway for cyclaniliprole metabolism proceeds via hydrolysis of the amino-cyclopropane bond yielding YT-1284. YT-1284 can either undergo oxidative deamination at the carboxylic amide of the phenyl ring producing NSY-27, or alternatively it can undergo condensation or tautomerization yielding NSY-28.
Toxicokinetics/ Metabolism Beagle Dog PMRA # 2502018	Dogs received a single oral gavage dose of 1 mg/kg bw cyclaniliprole (both radiolabels) in 0.5% aqueous CMC, for investigation of excretion, biliary elimination, toxicokinetics or tissue distribution. Animals were bile-duct cannulated and studied for 48 hours. Each dose group was comprised of a single animal. Absorption ranged from 30 to 49% of the AD. Excretion was not complete after 48 hours, ranging from 26 to 47%, and occurred mainly via the feces (23-43% of the AD). Elimination via the bile represented approximately 3% of the AD whereas urine was less than 1% of the AD. Levels of radioactivity in ♀ were slightly lower than in ♂. T_{max} ranged from 6 to 48 hours (high inter-animal variability). The AUC and half-life were not determined, as levels of radioactivity did not decline over the 48-hour study period. Highest radioactivity concentrations were noted in the plasma, whole blood, liver or fat. Significant amounts of radioactivity were identified in the carcass (25-46%).
Acute oral toxicity (Acute toxic class) Clr:CD SD Rat PMRA # 2398885	LD_{50} (♀) > 2000 mg/kg bw Low acute toxicity
Acute dermal toxicity	LD_{50} > 2000 mg/kg bw

Study Type/ Animal/ PMRA #	Study Results
Clr:CD SD Rat PMRA # 2398887	Low acute toxicity
Acute inhalation toxicity (nose-only) Wistar Hannover Rat PMRA # 2398888	LC_{50} > 4.62 mg/L Low acute toxicity
Eye irritation NZW Rabbit PMRA # 2398891	MIS (unrinsed) = 4 (1 hour) MAS (unrinsed) = 0 MIS (rinsed) = 2.67 (1 hour) MAS (rinsed) = 0 Non Irritating
Dermal irritation NZW Rabbit PMRA # 2398890	MAS = 0 MIS = 0 Not irritating
Dermal sensitization (Local Lymph Node Assay) CBA/J Mouse PMRA # 2398894	Not a dermal sensitizer
Dermal sensitization (Maximization test) Hartley Guinea Pig PMRA # 2398895	Not a dermal sensitizer
90-day oral toxicity (diet) CRL:CD1 Mouse PMRA # 2398900	NOAEL = 1023/1350 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the highest dose tested.
28-day oral toxicity (diet) Wistar Hannover Rat PMRA # 2398896	NOAEL and LOAEL not established as study considered supplemental (lack of histopathology) No adverse effects were observed up to the highest dose tested.
90-day oral toxicity (diet) Wistar Hannover Rat PMRA # 2398898	NOAEL = 1331/1594 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the highest dose tested.
90-day oral toxicity (diet)	NOAEL = 27/27 mg/kg bw/day in ♂/♀

Study Type/ Animal/ PMRA #	Study Results
Beagle Dog PMRA # 2398904	Effects at the LOAEL (266/270 mg/kg bw/day in ♂/♀): ↑liver wt, ↑ALP (♂/♀); liver centrilobular hepatocellular hypertrophy, ↓ albumin (♂)
1-year oral toxicity (diet) Beagle Dog PMRA # 2398905	NOAEL = 27/28 mg/kg bw/day in ♂/♀ Effects at the LOAEL(259/288 mg/kg bw/day in ♂/♀): ↑ALP, ↓ albumin, liver centrilobular hepatocellular hypertrophy (♂/♀); ↑ liver wt (♂)
28-day dermal toxicity Sprague-Dawley Rat PMRA # 2398908	NOAEL = 1000 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the highest dose tested.
Subchronic inhalation toxicity PMRA # 2444521	Study waiver rationale accepted on the basis of low acute inhalation toxicity, low overall repeat-dose toxicity, and the margins of exposure calculated when using a toxicological endpoint from an oral toxicity study.
1-year oral toxicity (diet) Wistar Hannover Rat PMRA # 2398913	NOAEL = 955/1213 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the highest dose tested. No evidence of oncogenicity
2-year combined chronic toxicity /oncogenicity (diet) Wistar Hannover Rat PMRA # 2398914	NOAEL = 834/1041 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the highest dose tested. No evidence of oncogenicity
18-month oncogenicity study (diet) CD1 Mouse PMRA # 2398915	NOAEL = 884/1316 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the highest dose tested. No evidence of oncogenicity
2-generation reproductive toxicity (diet) Sprague-Dawley Rat PMRA # 2398916, 2398917	Parental NOAEL = 1046/1589 mg/kg bw/day in ♂/♀ Offspring NOAEL =1589 mg/kg bw/day Reproductive NOAEL = 1046/1589 mg/kg bw/day in ♂/♀ LOAELs not established as no adverse effects were observed up to the highest dose tested. No evidence of sensitivity of the young

Study Type/ Animal/ PMRA #	Study Results
Developmental toxicity (gavage) Wistar Hannover Rat PMRA #2398918, 2398919	Maternal NOAEL = 1000 mg/kg bw/day Developmental NOAEL = 1000 mg/kg bw/day LOAELs not established as no adverse effects were observed up to the highest dose tested. No evidence of sensitivity of the young
Developmental toxicity (gavage) Japanese White Rabbit PMRA #2389820, 2389822	Maternal NOAEL = 1000 mg/kg bw/day Developmental NOAEL = 1000 mg/kg bw/day LOAELs not established as no adverse effects were observed up to the highest dose tested. No evidence of sensitivity of the young
Bacterial reverse mutation Salmonella typhimurium strains TA 98, TA 100, TA 1535 or TA 1537; Escherichia coli strain WP2 uvrA PMRA # 2398909	Negative.
In vitro gene mutation in mammalian cells Mouse lymphoma cells PMRA # 2398911	Negative.
In vitro chromosome aberration Chinese hamster cells PMRA # 2398910	Negative.
In vivo micronucleus assay Crlj:CD1 Mouse (♂) PMRA # 2398912	Negative.
Acute neurotoxicity (gavage) Sprague-Dawley Rat PMRA# 2398923	NOAEL = 2000 mg/kg bw LOAEL not established as no adverse effects were observed up to the highest dose tested.
90-day neurotoxicity (diet) Sprague-Dawley Rat	NOAEL = 1085/1279 mg/kg bw/day in ♂/♀ LOAEL not established as no adverse effects were observed up to the

Study Type/ Animal/ PMRA #	Study Results
PMRA# 2398924	highest dose tested.
28-day imunotoxicity (diet) CRL:CD1 Mouse PMRA # 2398884	NOAEL = 1352 mg/kg bw/day ↓ PFC/10^6 spleen cells, not statistically significant; high intra-group variability (equivocal)
Studies on NK-1375 (rat metabolite and photo-degradation product)	
Acute oral toxicity (acute toxic class) Clr:CD SD Rat PMRA # 2398886	LD_{50} (♀) > 2000 mg/kg bw
Bacterial reverse mutation Salmonella typhimurium strains TA 98, TA 100, TA 1535 or TA 1537; Escherichia coli strain WP2 uvrA PMRA # 2398909	Negative

Table 5 Toxicology Endpoints for Use in Human Health Risk Assessment for Cyclaniliprole

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary (ARfD)	Not required as no endpoint of concern attributable to a single exposure was identified.		
Repeated dietary	90-day and 1-year dietary toxicity studies in the dog (combined results)	NOAEL = 27 mg/kg bw/day Increased liver weight and ALP, decreased albumin, centrilobular hepatocellular hypertrophy	100
	ADI = 0.3 mg/kg bw/day		
Short- and intermediate-term dermal	28-day dermal toxicity study in the rat	NOAEL = 1000 mg/kg bw/day No adverse effects noted at the highest dose tested	100
Short- and intermediate-term inhalation[2]	90-day dietary toxicity study in the dog	NOAEL = 27 mg/kg bw/day Increased liver weight and ALP, decreased albumin, centrilobular hepatocellular hypertrophy	100
Cancer	Not required since there was no evidence of oncogenicity		

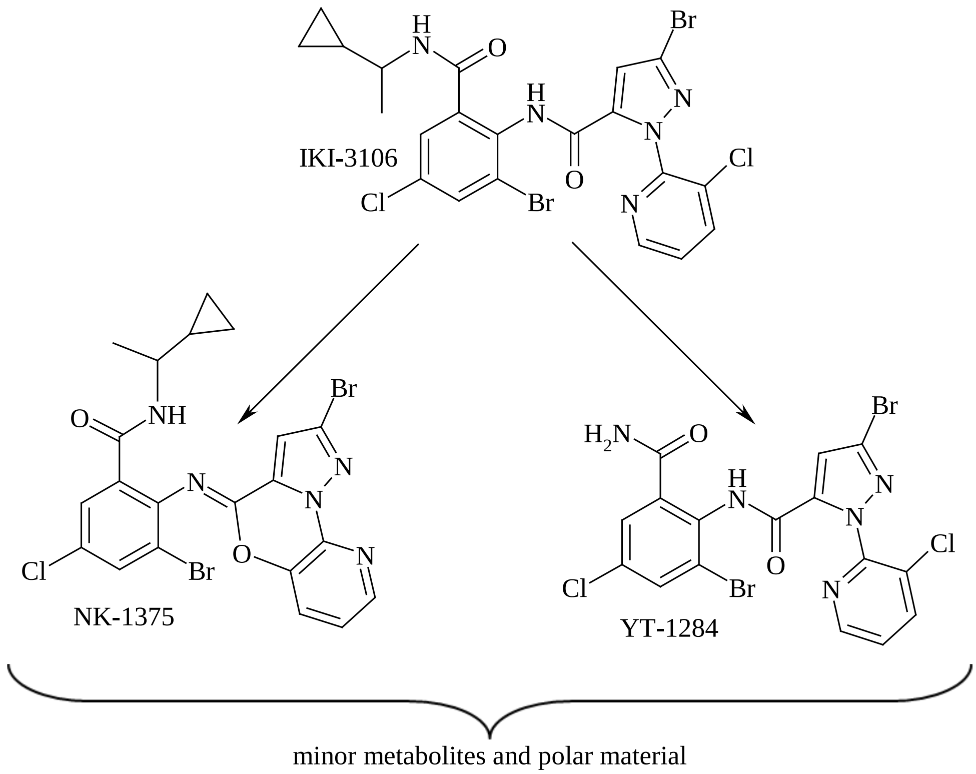
[1] CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments.

[2] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 6 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN APPLES				**PMRA #2398928**
Radiolabel Position	$[^{14}C$-phenyl]-cyclaniliprole and $[^{14}C$-pyrazole]-cyclaniliprole			
Test Site	Two trees selected from a mature orchard were used. The canopies were pruned slightly to provide suitable treatment areas (approximately 2 m^2) which were enclosed with plastic sheeting. Selected fruit were protected from exposure to the spray to allow assessment of the extent of translocation.			
Treatment	Foliar treatment			
Total Rate	3 × 100 g a.i./ha; total rate of 300 g a.i./ha			
Formulation	Liquid formulation			
Preharvest interval	15 days (immature harvest, BBCH 81) and 30 days (mature harvest, BBCH 89)			
Matrices	**PHI (days)**	**$[^{14}C$-phenyl]**	**$[^{14}C$-pyrazole]**	
		TRRs (ppm)	**TRRs (ppm)**	
Fruit (surface wash)	15	0.137	0.099	
	30	0.025	0.023	
Fruit (flesh)	15	0.003	0.011	
	30	0.005	0.003	
Fruit (peel)	15	0.008	0.024	
	30	0.012	0.010	
Fruit (total)	15	0.148	0.135	
	30	0.042	0.036	
Leaves	15	18.87	11.21	
	30	8.17	5.42	
Metabolites Identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**$[^{14}C$-phenyl]**	**$[^{14}C$-pyrazole]**	**$[^{14}C$-phenyl]**	**$[^{14}C$-pyrazole]**
Immature fruit (Day 15)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	YT-1284	YT-1284
Mature fruit (Day 30)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	YT-1284	YT-1284
Leaves (Day 15)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	YT-1284	YT-1284
Leaves (Day 30)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	YT-1284	YT-1284

Proposed Metabolic Scheme in Apples



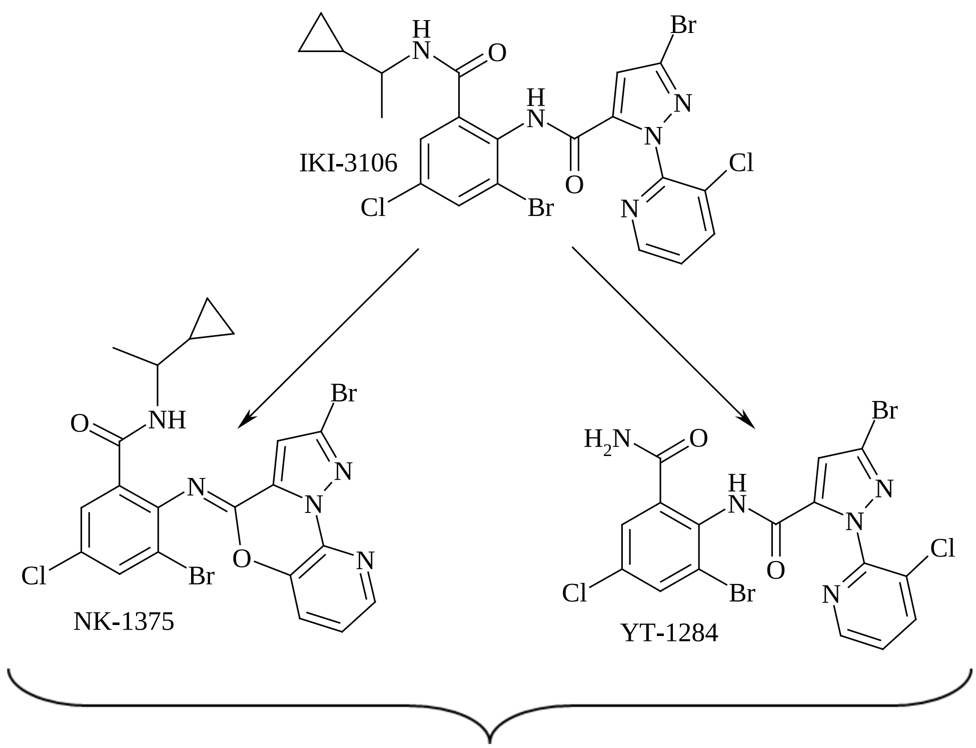
When applied as a foliar (surface) treatment, cyclaniliprole (IKI-3106) undergoes very little translocation (residues on/in protected fruit <0.001 ppm). The metabolic pathway of cyclaniliprole in apples involves either intramolecular cyclization resulting in the predominant metabolite NK-1375, or hydrolysis of the amino-cyclopropane bond yielding the less prevalent metabolite YT-1284.

NATURE OF THE RESIDUE IN LETTUCE	**PMRA #2398926**
Radiolabel Position	[^{14}C-phenyl]-cyclaniliprole and [^{14}C-pyrazole]-cyclaniliprole
Test Site	Lettuce plants were grown in compost to maturity in a plastic polytunnel outdoors
Treatment	Foliar treatment
Total Rate	3 × 100 g a.i./ha; total rate of 300 g a.i./ha
Formulation	Liquid formulation
Preharvest interval	8 days (immature harvest, BBCH 46) and 15 days (mature harvest, BBCH 49)

Matrices	**PHI (days)**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
		TRRs (ppm)	**TRRs (ppm)**
Lettuce plant (surface wash)	8	0.637	0.638
	15	0.300	0.287
Lettuce plant (homogenized sample)	8	0.119	0.127
	15	0.093	0.084
Lettuce plant (total)	8	0.756	0.765
	15	0.393	0.371

Metabolites Identified	Major Metabolites (>10% of the TRRs)		Minor Metabolites (<10% of the TRRs)	
Radiolabel Position	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
Immature lettuce (Day 8)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	YT-1284	YT-1284
Mature lettuce (Day 15)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	YT-1284	YT-1284

Proposed Metabolic Scheme in Lettuce



minor metabolites and polar material

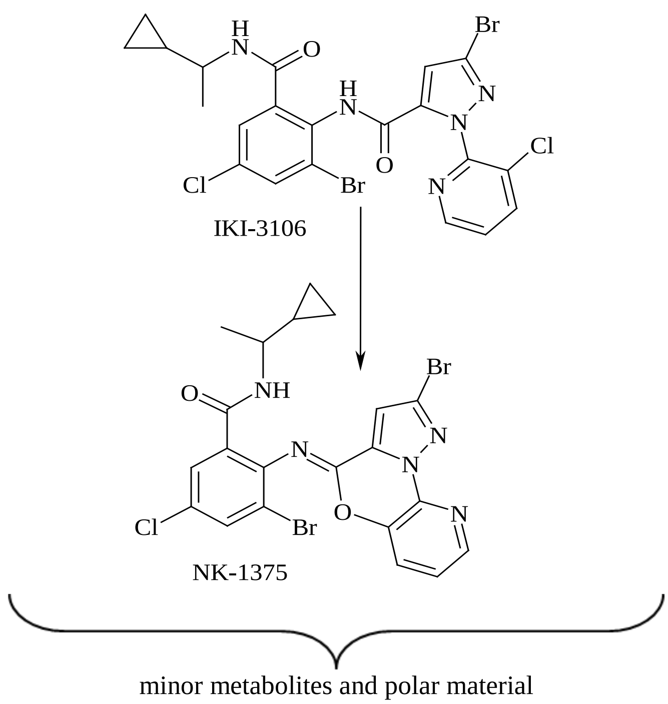
The metabolic pathway of cyclaniliprole (IKI-3106) in lettuce involves either intramolecular cyclization resulting in the predominant metabolite NK-1375, or hydrolysis of the amino-cyclopropane bond yielding the less prevalent metabolite YT-1284.

NATURE OF THE RESIDUE IN POTATOES	PMRA #2398927		
Radiolabel Position	[^{14}C-phenyl]-cyclaniliprole and [^{14}C-pyrazole]-cyclaniliprole		
Test Site	Eight pots, each containing a plant grown from a single seed potato, were assigned to two groups of eight plants. Each group was arranged to give an area of approximately 1 m^2 (8 plants/m^2). The pots were maintained outdoors, under netting.		
Treatment	Foliar treatment		
Total Rate	3 × 40 g a.i./ha; total rate of 120 g a.i./ha		
Formulation	Liquid formulation		
Preharvest interval	8 days (immature harvest, BBCH 96) and 15 days (mature harvest, BBCH 99)		
Matrices	**PHI (days)**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
		TRRs (ppm)	**TRRs (ppm)**
Tubers*	8	0.001	0.002
	15	0.001	0.002

Leaves (surface wash)	8	1.275	1.722
	15	0.949	0.686
Leaves (homogenized foliage)	8	1.084	1.301
	15	0.852	0.888
Leaves (total)	8	2.359	3.023
	15	1.801	1.574
* No characterization of the residues was carried out for tubers as the TRRs were below 0.01 ppm.			

Metabolites Identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
Leaves (Day 8)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	--	--
Leaves (Day 15)	Cyclaniliprole, NK-1375	Cyclaniliprole, NK-1375	--	--

Proposed Metabolic Scheme in Potatoes



When applied as a foliar (surface) treatment, cyclaniliprole (IKI-3106) undergoes very little translocation. The metabolic pathway of cyclaniliprole in potatoes involves intramolecular cyclization resulting in the predominant metabolite NK-1375.

CONFINED ACCUMULATION IN ROTATIONAL CROPS – Lettuce, carrot and wheat	**PMRA # 2399211**
Radiolabel Position	[^{14}C-phenyl]-cyclaniliprole
Test site	Wheat, carrot and lettuce were sown in soil in plastic pots maintained in indoor controlled environment rooms and grown to maturity.
Formulation	Soluble concentrate
Application rate and timing	Bare soil was treated at 100 g a.i./ha, and aged for 30, 120 and 365 days.

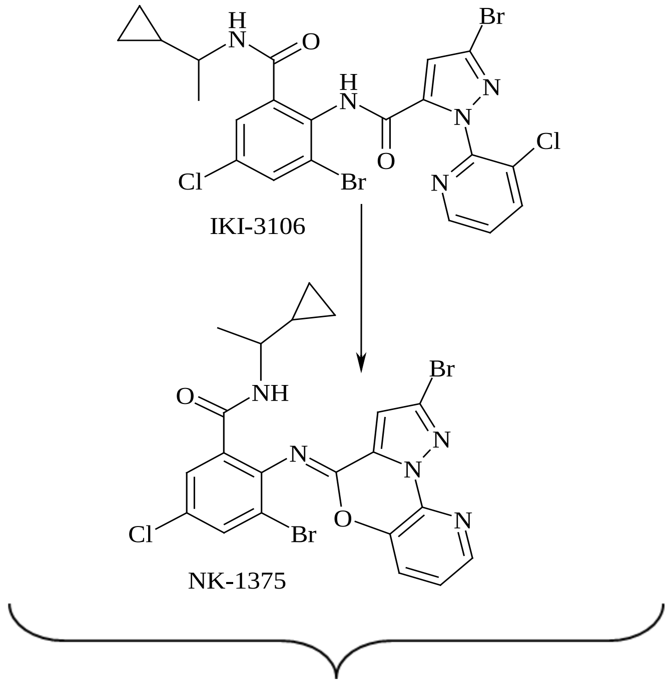
The TRR in soil sampled at the end of each ageing period and at the final harvest for each crop were in the range 0.027 – 0.071 ppm with no overall trend.

TRR in lettuce grown in soil aged for 30 or 120 days were 0.001 ppm at both the immature and mature harvests. TRR in carrots grown in soil aged for 30 or 120 days were in the range 0.001 – 0.002 ppm at both the immature and mature harvests. For both lettuce and carrots, concentrations in samples were below the trigger value of 0.01 ppm and as such required no further characterization.

In wheat grown in soil aged for 30 days, the TRR increased from 0.018 ppm in the forage to 0.030 ppm in the hay and 0.058 ppm in the straw. The TRR in the grain was 0.001 ppm which is below the trigger value of 0.01 ppm and as such required no further characterization. TRR in wheat grown in soil aged for 120 days were similar to those obtained from wheat grown in soil aged for 30 days (0.018 ppm in the forage, 0.028 ppm in the hay and 0.059 ppm in the straw). The TRR in the grain was below the limit of detection (<0.0005 ppm). TRR in wheat grown in soil aged for 365 days were lower than those observed from the shorter plantback intervals (0.015 ppm in the forage, 0.017 ppm in the hay and 0.029 ppm in the straw). The TRR in the grain was below the limit of detection.

Metabolites Identified		**Major Metabolites (>10% of the TRRs)**	**Minor Metabolites (<10% of the TRRs)**
Matrices	**PBI (days)**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
Wheat forage	30	Cyclaniliprole, NK-1375	--
	120	Cyclaniliprole	NK-1375
	365	Cyclaniliprole	NK-1375
Wheat hay	30	Cyclaniliprole	NK-1375
	120	Cyclaniliprole	NK-1375
	365	Cyclaniliprole	NK-1375
Wheat straw	30	Cyclaniliprole	--
	120	Cyclaniliprole	NK-1375
	365	Cyclaniliprole	NK-1375

Proposed Metabolite Scheme in Rotational Crops



minor metabolites and polar material

Cyclaniliprole (IKI-3106), when applied to soil, undergoes limited uptake into planted secondary crops. Any compound taken up undergoes very little metabolism. However, when metabolized, cyclaniliprole undergoes nucleophilic aromatic substitution yielding the primary metabolite, NK-1375.

NATURE OF THE RESIDUE IN LAYING HEN	**PMRA #2398929**

Twenty laying hens (10 animals per radiolabel) were dosed orally with [^{14}C-phenyl]-cyclaniliprole or [^{14}C-pyrazole]-cyclaniliprole at 0.6 – 0.9 mg/kg bw/day (corresponding to 11.3 and 10.8 ppm in feed, respectively) by gelatin capsule once daily for 14 days. Samples of excreta were collected twice daily and cage washes were conducted daily. Samples of eggs were collected twice daily. The hens were euthanized 12 hours after administration of the final dose.

Matrices	**[^{14}C-phenyl]**		**[^{14}C-pyrazole]**	
	TRRs (ppm)	**% of Administered Dose**	**TRRs (ppm)**	**% of Administered Dose**
Excreta	--	91.7	--	92.9
Cage wash	0.11	1.0	0.15	1.4
Leg muscle	0.088	<0.3*	0.075	<0.3*
Breast muscle	0.056		0.058	
Abdominal fat	0.347		0.276	
Subcutaneous fat	0.337		0.262	
Skin	0.269		0.304	
Liver	1.659	0.5	1.466	0.4
Eggs	0.695**	2.0	0.668*	2.5

* For both radiolabels, TRRs in fat, muscle and skin collected at sacrifice were collectively <0.3% of the administered dose.
** The TRRs reported for eggs is from the pooled sample, days 9-14.

Metabolites identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
Egg	Cyclaniliprole, NSY-28	Cyclaniliprole, NSY-28	NSY-27, YT-1284	NSY-27, YT-1284
Fat	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, NSY-28	NSY-27	NSY-27, YT-1284
Skin	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, NSY-28, YT-1284	NSY-27	NSY-27
Muscle	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, NSY-28, YT-1284	NSY-27	NSY-27
Liver	NSY-28	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, YT-1284, NSY-27	NSY-27

NATURE OF THE RESIDUE IN LACTATING GOAT — **PMRA # 2398930**

Two lactating goats were dosed orally with [^{14}C-phenyl]-cyclaniliprole or [^{14}C-pyrazole]-cyclaniliprole at doses at 0.37 – 0.41 mg/kg bw/day (corresponding to 12.3 and 11.2 ppm in feed, respectively) by gelatin capsule once daily for 5 days. Samples of excreta were collected twice daily and cage washes were conducted daily. Milk was collected twice daily. The goats were euthanized 23 hours after administration of the final dose.

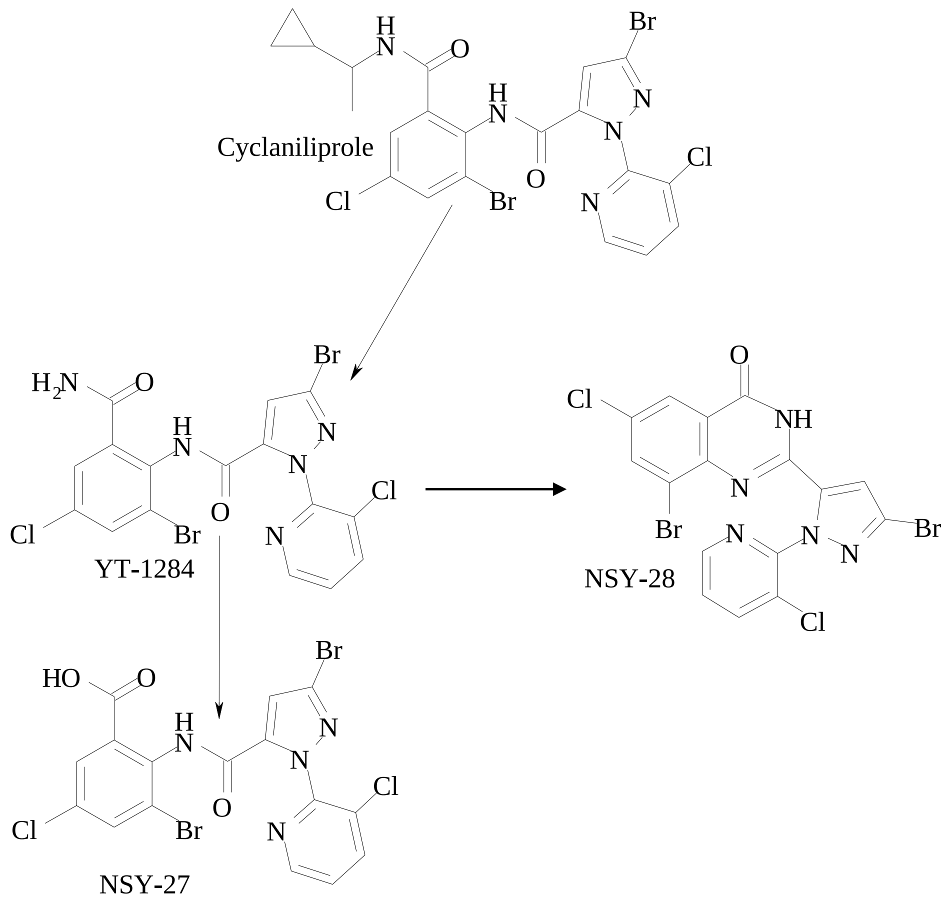
Matrices	**[^{14}C-phenyl]**		**[^{14}C-pyrazole]**	
	TRRs (ppm)	**% of Administered Dose**	**TRRs (ppm)**	**% of Administered Dose**
Urine + cage wash	--	5.3	--	6.9
Feces	--	67.7	--	59.0
GI tract	--	5.4	--	9.5
Bile	--	<0.1	--	<0.1
Loin muscle	0.125	2.3	0.118	1.6
Flank muscle	0.118		0.103	
Omental fat	0.860	3.9	0.634	2.2
Perirenal fat	0.821		0.786	
Subcutaneous fat	0.857		0.445	
Kidney	0.582	0.1	0.547	0.1
Liver	1.485	1.7	1.321	1.4
Milk	0.131*	0.8	0.082*	0.7

* For the [^{14}C-phenyl] label, the TRR value is from the pooled sample of the whole milk for Days 4-5.
For the [^{14}C-pyrazole] label, the TRR value is from the pooled sample of the whole milk for Days 2-5.

Metabolites identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**	**[^{14}C-phenyl]**	**[^{14}C-pyrazole]**
Liver	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, NSY-28, YT-1284	NSY-27	NSY-27
Kidney	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, NSY-28, YT-1284	NSY-27	NSY-27
Muscle	Cyclaniliprole, NSY-28, YT-1284	Cyclaniliprole, NSY-28, YT-1284	--	--
Fat	Cyclaniliprole	Cyclaniliprole, NSY-28	NSY-28, YT-1284, NSY-27	YT-1284
Whole milk	Cyclaniliprole, YT-1284	Cyclaniliprole, YT-1284	NSY-28, NSY-27	NSY-28, NSY-27
Milk fat	Cyclaniliprole	Cyclaniliprole	NSY-28, YT-1284, NSY-27	NSY-28, YT-1284, NSY-27

Milk aqueous	Cyclaniliprole, YT-1284	Cyclaniliprole, YT-1284, NSY-28	NSY-28, NSY-27	NSY-27

Proposed Metabolic Scheme in Livestock



Metabolism of cyclaniliprole proceeds via hydrolysis of amino-cyclopropane bond yielding YT-1284. YT-1284 can either undergo hydrolysis at the carboxylic amide of the phenyl ring producing NSY-27, or alternatively intramolecular cyclization yielding NSY-28.

FREEZER STORAGE STABILITY	PMRA #2444537

Plant matrices: Wine, oilseed rape seeds, grapes, lettuce, potatoes, broccoli and dry beans
The freezer storage stability data indicate that residues of cyclaniliprole and the metabolite NK-1375 are stable at -20°C for 18 months. These matrices represent high oil, high acid, high water, high starch, and high protein content; thus cyclaniliprole is stable in all plant and processed commodities for 18 months.

Animal matrices: Not required for poultry commodities as there are no poultry feeding studies. For cattle, concurrent freezer storage stability analyses were conducted for edible tissues as part of the dairy cattle feeding study. Milk samples (whole, cream and skimmed) from the feeding study were stored for less than 30 days between sampling and analysis. Therefore, freezer storage stability data are not required for these matrices.

CROP FIELD TRIALS & RESIDUE DECLINE ON POME FRUIT	PMRA #2399208, 2399198

Field trials on apples were conducted in 2012 in Canada and the United States. Ten trials were conducted in NAFTA Growing Regions 1 (2 trials), 2 (1 trial), 5 (3 trials), 9 (1 trial), 10 (1 trial) and 11 (2 trials). IKI-3106 50 SL, a soluble concentrate formulation containing cyclaniliprole, was applied three times as airblast sprays at a rate of ~100 g a.i./ha/application for seasonal application rates of 297 - 461 g a.i./ha (~1 – 1.5x GAP). An adjuvant was not added to the spray mixture for any of the trials. The applications were made at 14±1 -day intervals with the last application occurring 6-7 days before harvest. In two trials, additional samples were collected at PHIs of 0, 3, and 10 days to monitor residue decline. Residue decline data show that residues of cyclaniliprole in apples decrease with increasing PHIs. Decline behaviour could not be evaluated for the metabolite NK-1375 as all residues were non quantifiable (i.e., <LOQ).

In addition, field trials on apples and pears were conducted in 2013 in Canada and the United States. Seven trials on apples were conducted in NAFTA Growing Regions 1 (1 trial), 5 (4 trials), and 11 (2 trials). Nine trials on pears were conducted in NAFTA Growing Regions 1 (1 trial), 5 (3 trials), 10 (2 trials), and 11 (3 trials). At each trial location, IKI-3106 50 SL, a soluble concentrate formulation, was applied as airblast sprays at ~100 g a.i./ha/application for seasonal application rates of 296 – 337 g a.i./ha (~1 – 1.1x GAP). An adjuvant was not added to the spray mixture, except for one apple trial and one pear trial. The applications were made at 14±1 -day intervals with the last application occurring 6-8 days before harvest. In one pear trial, additional samples were collected at PHIs of 1, 4 and 10 days. Residue decline data show that residues of cyclaniliprole decrease in pears with increasing PHIs while residues of metabolite NK-1375 remain about the same. Residues in apple and pear samples harvested from the sites in which an adjuvant was included in the spray applications were comparable to residues observed from the samples not treated with an adjuvant.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Apple fruit	297 – 461	6-8	17	0.012	0.132	0.054	0.055	0.032
Pear fruit	296 – 337	6-7	9	0.036	0.142	0.097	0.096	0.036
NK-1375 (expressed as parent equivalents)								
Apple fruit	297 – 461	6-8	17	0.011	0.035	0.011	0.014	0.006
Pear fruit	296 – 337	6-7	9	0.011	0.024	0.015	0.016	0.004

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** An adjuvant was not added to the spray mixture, except for one apple trial and one pear trial.

CROP FIELD TRIALS & RESIDUE DECLINE ON CUCURBIT VEGETABLES | **PMRA #2399194**

Field trials were conducted in 2013 in Canada and the United States. Ten trials on cantaloupe were conducted in NAFTA Growing Regions 2 (1 trial), 5 (5 trials), 6 (1 trial), and 10 (3 trials) Nine trials on cucumbers were conducted in NAFTA Growing Regions 2 (2 trials), 3 (1 trial), 5 (5 trials), and 6 (1 trial). Nine trials on summer squash were conducted in NAFTA Growing Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (4 trials), 10 (1 trial) and 12 (1 trial). IKI-3106 50 SL, a soluble concentrate formulation containing cyclaniliprole, was applied three times as foliar broadcast sprays at a rate of ~80 g a.i./ha/application for seasonal application rates of 237 - 249 g a.i./ha (~1x GAP). An adjuvant (a non-ionic surfactant) was added to the spray mixture for all applications at all trials, with the exception of 1 trial each for cucumber, summer squash and cantaloupe. The applications were made at 7±1 -day intervals with the last application occurring 1 day before harvest.

In one trial for each crop, additional samples were collected at PHIs of 0, 4, and 7 days to monitor residue decline. Residue decline data show that residues of cyclaniliprole decrease in cucumber, summer squash, and cantaloupe with increasing PHIs. Residues of NK-1375 decreased in cantaloupe between 0 and 7 days. Residues of NK-1375 were too low in cucumber and summer squash to determine residue decline. Residues in samples from crops treated with and without adjuvant were comparable.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Cantaloupe fruit	239 – 244	1	10	0.014	0.087	0.041	0.043	0.023
Cucumber fruit	237 – 249	1	9	0.010	0.025	0.014	0.016	0.006

Summer squash fruit	237 – 245	1	9	0.010	0.046	0.026	0.023	0.012
NK-1375 (expressed as parent equivalents)								
Cantaloupe fruit	239 – 244	1	10	0.011	0.018	0.011	0.012	0.002
Cucumber fruit	237 – 249	1	9	0.011	0.011	0.011	0.011	NA
Summer squash fruit	237 – 245	1	9	0.011	0.011	0.011	0.011	NA

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** An adjuvant (a non-ionic surfactant) was added to the spray mixture for all applications at all trials, with the exception of 1 trial each for cucumber, summer squash and cantaloupe.

CROP FIELD TRIALS & RESIDUE DECLINE ON TREE NUTS | **PMRA #2399193**

Field trials were conducted in 2012 in the United States. Five trials on almonds were conducted in NAFTA Growing Regions 10. Five trials on pecans were conducted in NAFTA Growing Regions 2 (2 trials), 4 (1 trial), 6 (1 trial), and 8 (1 trial). IKI-3106 50 SL, a soluble concentrate formulation containing cyclaniliprole, was applied three times as airblast sprays at a rate of ~100 g a.i./ha/application for seasonal application rates of 299 - 301 g a.i./ha (~1x GAP). An adjuvant was not added to the spray mixture of any of the applications. The applications were made at 14±1 -day intervals with the last application occurring 30-31 days before harvest.

In one trial for each crop, additional samples were collected at PHIs of 20, 25, and 39/40 days to monitor residue decline. Residues in almond and pecan nutmeats were too low to determine decline behaviour. For almond hulls, the decline study indicates that the level of cyclaniliprole and the metabolite NK-1375 decline with longer PHIs.

Commodity	Total Application Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Almond hulls	299 – 301	30 – 31	5	1.460	2.780	1.820	1.956	0.540
Almond nuts	299 – 301	30 – 31	5	0.010	0.014	0.013	0.012	0.002
Pecan nuts	299 – 310	29 – 30	3	0.010	0.010	0.010	0.010	NA
NK-1375 (expressed as parent equivalents)								
Almond hulls	299 – 301	30 – 31	5	0.252	0.738	0.418	0.465	0.193
Almond nuts	299 – 301	30 – 31	5	0.011	0.011	0.011	0.011	NA
Pecan nuts	299 – 310	29 – 30	3	0.011	0.011	0.011	0.011	NA

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation, NA = not applicable. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.

CROP FIELD TRIALS & RESIDUE DECLINE ON LEAFY VEGETABLES | **PMRA #2399197, 2399195**

Field trials were conducted in 2012 in Canada and the United States. Nine trials on head lettuce were conducted in NAFTA Growing Regions 1 (1 trial), 3 (1 trial), 5 (3 trials) and 10 (4 trials). Eleven trials on leaf lettuce were conducted in Regions 2 (1 trial), 3 (1 trial), 5 (5 trials), and 10 (4 trials). Eight trials on spinach were conducted in Regions 1 (1 trial), 2 (1 trial), 5 (2 trials), 6 (1 trial), 9 (1 trial), and 10 (2 trials). Five trials on mustard greens were conducted in Regions 2, 4, 5, 6, and 10 (1 trial per Region). At each trial location, IKI-3106 50 SL, a soluble concentrate formulation containing cyclaniliprole, was applied three times as foliar broadcast sprays at a rate of ~60 or ~80 g a.i./ha/application for seasonal application rates of 181 - 247 g a.i./ha (0.75 – 1x GAP). An adjuvant was added to the spray mixture for all applications at most sites, except for 1 head lettuce trial and 1 leaf lettuce trial, both in Region 3, and 1 mustard green trial in Region 4. The applications were made at 7±1 -day intervals with the last application occurring 0-1 days before harvest.

In one leaf lettuce trial and one mustard green trial, samples were collected at PHIs of 0, 1, 3, and 7 days to monitor residue decline. Residue decline data show that residues of cyclaniliprole and NK-1375 decrease in leaf lettuce and mustard greens with increasing PHIs. In general, residues in samples from crops treated with and without adjuvant were comparable.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Head lettuce with wrapper leaves	185 – 247	1	9	0.067	2.160	0.559	0.764	0.699
Head lettuce without wrapper leaves	185 – 247	1	9	0.010	0.708	0.086	0.194	0.266
Leaf lettuce leaves	183 – 246	1	11	0.246	2.980	1.240	1.409	0.863
Spinach leaves	181 – 245	0-1	8	1.380	4.610	2.555	2.680	0.987
Mustard green leaves	181 – 240	1	5	1.410	5.900	3.960	3.686	1.640
NK-1375 (expressed as parent equivalents)								
Head lettuce with wrapper leaves	185 – 247	1	9	0.013	0.256	0.050	0.100	0.086
Head lettuce without wrapper leaves	185 – 247	1	9	0.011	0.113	0.011	0.027	0.034
Leaf lettuce leaves	183 – 246	1	11	0.023	0.378	0.110	0.148	0.118
Spinach leaves	181 – 245	0-1	8	0.074	0.934	0.309	0.403	0.313
Mustard green leaves	181 – 240	1	5	0.106	0.434	0.340	0.313	0.123

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** An adjuvant was used in the spray applications at all trials except for 1 trial for each of head and leaf lettuce and mustard greens.

CROP FIELD TRIALS & RESIDUE DECLINE ON BRASSICA HEAD AND STEM VEGETABLE GROUP — **PMRA #2399195**

Field trials were conducted in 2012 in Canada and the United States. Ten trials on cabbage were conducted in NAFTA Growing Regions 1 (1 trial), 2 (1 trial), 3 (1 trial), 5 (5 trials), 6 (1 trial) and 10 (1 trial). Ten trials on broccoli were conducted in NAFTA Growing Regions 5 (4 trials), 6 (1 trial), 10 (4 trials), and 12 (1 trial). At each trial location, IKI-3106 50 SL, a soluble concentrate formulation containing cyclaniliprole, was applied as broadcast foliar sprays at ~60 or ~80 g a.i./ha/application for seasonal application rates of 183 – 299 g a.i./ha (~0.8 – 1.2x GAP). An adjuvant was added to the spray mixture, except for 3 cabbage trials and 1 broccoli trial. The applications were made at 7±1 -day intervals with the last application occurring 1 day before harvest.

In one trial for each crop, additional samples were collected at PHIs of 0, 3 and 7 days for cabbage and at PHIs of 3, 5 and 7 days for broccoli to monitor residue decline. Residue decline data show that residues of cyclaniliprole and the metabolite NK-1375 decrease in cabbage and broccoli with increasing PHIs. In general, residues in samples from crops treated with and without adjuvant were comparable.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Cabbage head	183 – 299	1	10	0.010	0.392	0.033	0.106	0.139
Broccoli head and stem	183 – 250	1	10	0.110	0.660	0.357	0.327	0.176
NK-1375 (expressed as parent equivalents)								
Cabbage head	183 – 299	1	10	0.011	0.030	0.011	0.015	0.006
Broccoli head and stem	183 – 250	1	10	0.011	0.077	0.023	0.032	0.025

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** An adjuvant was used in the spray applications at all trials except for 3 cabbage trials and 1 broccoli trial.

CROP FIELD TRIALS & RESIDUE DECLINE ON FRUITING VEGETABLES — **PMRA #2399207**

Field trials were conducted in 2012 in Canada and the United States. Twenty-one trials on tomatoes, including 2 trials on small varieties, were conducted in NAFTA Growing Regions 1 (1 trial), 2 (1 trial), 3 (2 trial), 5 (12 trials), and 10 (6 trials). Nine trials on bell peppers were conducted in Regions 2 (1 trials), 3 (1 trial), 5 (4 trials), 6 (1 trial) and 10 (2 trials). Three trials on non-bell peppers were conducted in Regions 3, 5, and 10 (1 trial per Region). At each trial location, IKI-3106 50 SL, a soluble concentrate containing cyclaniliprole, was applied three times as foliar broadcast sprays at a rate of ~60 or ~80 g a.i./ha/application for seasonal application rates of 180 – 260 g a.i./ha (~0.75 – 1.1x GAP). An adjuvant was added to the spray mixture for all applications, expect for 10 of the 21 tomato trials. The applications were made at 7±1 -day intervals with the last application occurring 1 day before harvest, except for one tomato trial in Region 10 (PHI of 4 days). The results of two tomato trials in Region 5 were combined and considered as one study, as the trials were conducted at the same site at the same time on the same variety.

In two trials on tomatoes and one trial on bell peppers, additional samples were collected at PHIs of 0, 3 and 7 days to monitor residue decline. Residue decline data from one tomato study and one bell pepper study show that residues of cyclaniliprole decrease in tomatoes and bell peppers with increasing PHIs, while residues of NK-1375 were too low to assess decline. In a second tomato decline study, all residues were too low to assess decline. In general, residues in samples from crops treated with and without adjuvant were comparable.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Tomato fruit	180 – 260	1	21	0.011	0.076	0.029	0.032	0.016
Bell pepper fruit	180 – 245	1	9	0.014	0.101	0.048	0.055	0.032
Non-bell pepper fruit	234 – 240	1	3	0.041	0.077	0.057	0.058	0.018
NK-1375 (expressed as parent equivalents)								
Tomato fruit	180 – 260	1	21	0.011	0.027	0.011	0.012	0.003
Bell pepper fruit	180 – 245	1	9	0.011	0.027	0.011	0.014	0.005
Non-bell pepper fruit	234 – 240	1	3	0.011	0.017	0.011	0.013	0.003

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** An adjuvant was added to the spray mixture for all applications, expect for 10 of the 21 tomato trials.

CROP FIELD TRIALS & RESIDUE DECLINE ON STONE FRUITS — **PMRA #2399206**

Field trials were conducted in 2013 in Canada and the United States. Twelve trials on peaches were conducted in NAFTA Growing Regions 1 (1 trial), 2 (3 trials), 5 (3 trials), 6 (1 trial), 10 (3 trials), and 11 (1 trial). Seven trials on plums were conducted in Regions 5 (1 trial), 10 (4 trials), 11 (1 trial), and 12 (1 trial). Seven trials on sweet cherries were conducted in Regions 5 (1 trial), 9 (1 trial), 10 (2 trials) and 11 (3 trials). Six trials on tart cherries were conducted in Regions 1 (1 trial), 5 (3 trials), 9 (1 trial), and 14 (1 trial). At each trial location, IKI-3106 50 SL, a soluble concentrate containing cyclaniliprole, was applied three times as airblast sprays at a rate of ~100 g a.i./ha/application for seasonal application rates of 291 - 310 g a.i./ha (~1x GAP). An adjuvant was added to the spray mixture for all applications, expect for 3 peach trials, 2 plum trials, 3 sweet cherry trials, and 5 tart cherry trials. The applications were made at 7±1 -day intervals with the last application occurring 6-7 days before harvest.

In three trials, additional samples were collected at different time intervals (PHIs of 1, 4, and 10 days for peach and plum; and PHIs of 4, 10, and 14 days for tart cherry) to monitor residue decline. Residue decline data show that residues of IKI-3106 and total residues decrease in peaches, plums, and tart cherries with increasing PHIs. Although decline of NK-1375 in peaches and plums could not be assessed since all residues of NK-1375 were <LOQ in those decline studies, the tart cherry decline study shows that residues of NK-1375 decrease in tart cherries with increasing PHIs. Residues in samples

harvested from the sites in which an adjuvant was not included in the spray applications were comparable to residues observed from the samples treated with an adjuvant.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Peach fruit	293 – 307	6 – 7	12	0.022	0.191	0.059	0.080	0.050
Plum fruit	298 – 306	6 – 7	7	0.018	0.091	0.056	0.048	0.028
Sweet cherry fruit	295 – 310	6 – 7	7	0.097	0.329	0.142	0.187	0.091
Tart cherry fruit	291 – 307	6 – 7	6	0.082	0.562	0.262	0.291	0.182
NK-1375 (expressed as parent equivalents)								
Peach fruit	293 – 307	6 – 7	12	0.011	0.017	0.011	0.012	0.002
Plum fruit	298 – 306	6 – 7	7	0.011	0.018	0.011	0.012	0.003
Sweet cherry fruit	295 – 310	6 – 7	7	0.011	0.016	0.012	0.013	0.002
Tart cherry fruit	291 – 307	6 – 7	6	0.022	0.055	0.036	0.037	0.014

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** An adjuvant was added to the spray mixture for all applications, expect for 3 peach trials, 2 plum trials, 3 sweet cherry trials, and 5 tart cherry trials.

CROP FIELD TRIALS & RESIDUE DECLINE ON GRAPES — **PMRA #2399196**

Field trials were conducted in 2013 in Canada and the United States. Fifteen trials were conducted in NAFTA Growing Regions 1 (2 trials), 5 (3 trials), 10 (8 trials), and 11 (2 trials). IKI-3106 50 SL, a soluble concentrate formulation containing cyclaniliprole, was applied three times as airblast sprays at a rate of ~100 g a.i./ha/application for seasonal application rates of 296 - 309 g a.i./ha (~1.2 – 1.3x GAP). A nonionic surfactant was added for all applications at four sites. The applications were made at 7±1 -day intervals with the last application occurring 6-7 days before harvest.

In one trial, additional samples were collected at PHIs of 3, 5, and 9 days to monitor residue decline. Residue decline data show that residues of cyclaniliprole and NK-1375 decrease in grapes with increasing PHIs. Residues in samples harvested from the sites in which an adjuvant was not included in the spray applications were comparable to residues observed from the samples including an adjuvant.

Commodity	Total Application Rate (g a.i./ha)**	PHI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Grape fruit	296 – 309	6 - 7	15	0.024	0.508	0.134	0.176	0.137
NK-1375								
Grape fruit	296 – 309	6 - 7	15	0.011	0.116	0.016	0.039	0.041

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
** A nonionic surfactant was added for all applications at four sites.

RESIDUE DATA IN ROTATIONAL CROPS	PMRA #2399213, 2399212

Six field trials for cyclaniliprole on wheat as a rotational crop were conducted in the United States including Canadian representative growing regions encompassing NAFTA Growing Regions 1, 2, 5, 6, 10, and 11 (1 trial in each Region) during the 2012 growing season. At each trial location, one application of IKI-3106 50SL was made to a primary crop or weeds at 290 – 310 g a.i./ha. An adjuvant was not added to the spray mixture for any application. Prior to planting of the rotational crop, the cover crop was either tilled under the soil or killed with Roundup for a “no-till” planting. Wheat was planted into treated plots at plant-back intervals (PBIs) of 29/30, 119-127/120 and 147 -366 days.

In addition, three field trials for cyclaniliprole on wheat as a rotational crop were conducted after application to peppers and tomatoes in Europe. At each location, two applications of IKI-3106 50SL was made to the primary crop at a nominal rate of 40 g a.i./ha, 10-11 days apart for maximum rates of 81 – 86 g a.i./ha. No adjuvant was identified as being added to the spray mixture for any application. The treated crops were incorporated into the soil one day after the last application. Wheat was planted into the treated plots at PBIs of 29-32 days and 124-154 days.

Commodity	Total Application Rate (g a.i./ha)	PBI (days)	Residue Levels (ppm)					
			n	LAFT *	HAFT *	Median *	Mean *	SD *
Cyclaniliprole								
Wheat forage	290 – 310	29 – 30	5	0.010	0.014	0.013	0.013	0.002
		119 – 127	6	0.010	0.026	0.010	0.014	0.007
		147	1	0.010	0.010	0.010	0.010	N/A
		263	1	0.010	0.010	0.010	0.010	N/A
		356 – 366	3	0.010	0.021	0.010	0.014	0.006
Wheat grain		29 – 366	18	0.010	0.010	0.010	0.010	N/A
Wheat straw		29 – 30	5	0.010	0.067	0.027	0.034	0.023
		119 – 127	6	0.010	0.182	0.048	0.070	0.068
		147	1	0.036	0.036	0.036	0.036	N/A
		263	1	0.020	0.020	0.020	0.020	N/A
		356 – 366	3	0.010	0.082	0.022	0.038	0.039
Wheat forage	81 – 86	29 – 154	6	0.010	0.010	0.010	0.010	N/A
Wheat grain		29 – 154	6	0.010	0.010	0.010	0.010	N/A
Wheat hay		29 – 154	6	0.010	0.010	0.010	0.010	N/A
Wheat straw		29 – 154	6	0.010	0.010	0.010	0.010	N/A
NK-1375								
Wheat forage	290 - 310	29 – 30	5	0.011	0.011	0.011	0.011	N/A
		119 – 127	6	0.011	0.011	0.011	0.011	N/A
		147	1	0.011	0.011	0.011	0.011	N/A
		263	1	0.011	0.011	0.011	0.011	N/A
		356 – 366	3	0.011	0.011	0.011	0.011	N/A
Grain		29 – 366	18	0.011	0.011	0.011	0.011	N/A
Straw		29 – 30	5	0.011	0.011	0.011	0.011	N/A
		119 – 127	6	0.011	0.014	0.011	0.012	0.001
		147	1	0.011	0.011	0.011	0.011	N/A
		263	1	0.011	0.011	0.011	0.011	N/A
		356 – 366	3	0.011	0.011	0.011	0.011	N/A
Wheat forage	81 - 86	29 – 154	6	0.011	0.011	0.011	0.011	N/A

Wheat grain		29 – 154	6	0.011	0.011	0.011	0.011	N/A
Wheat hay		29 – 154	6	0.011	0.011	0.011	0.011	N/A
Wheat straw		29 – 154	6	0.011	0.011	0.011	0.011	N/A

* Values based on per-trial averages. LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation; NA = not applicable. For computation of the LAFT, HAFT, median, mean and standard deviation, values < LOQ are assumed to be at the LOQ (0.01 ppm for cyclaniliprole, 0.011 for NK-1375 expressed as parent equivalents).
n = number of independent field trials.
Based on the results of the field accumulation study, crops not on the label can be planted 30 days after application.

PROCESSED FOOD AND FEED - APPLE	**PMRA #2399208**	
Test Site	One trial in NAFTA Growing Region 5.	
Treatment	Broadcast foliar applications (3)	
Rate	3.00 kg a.i./ha	
End-use product/formulation	IKI-3106 50 SL	
Preharvest interval	7 days	
Processed Commodity	**Average Processing Factor**	
	Cyclaniliprole	**NK-1375**
Wet apple pomace	3.2x	3.2x
Apple juice	0.13x	0.13x

PROCESSED FOOD AND FEED – TOMATO	**PMRA #2399207**	
Test Site	One trial in NAFTA Growing Region 10.	
Treatment	Broadcast foliar applications (3)	
Rate	1.817 kg a.i./ha	
End-use product/formulation	IKI-3106 50 SL	
Preharvest interval	1 day	
Processed Commodity	**Average Processing Factor**	
	Cyclaniliprole	**NK-1375**
Tomato puree	0.23x	0.60
Tomato paste	0.46x	0.74x

PROCESSED FOOD AND FEED – PLUM	**PMRA #2399206**	
Test Site	One trial in NAFTA Growing Region 10.	
Treatment	Broadcast foliar applications (3)	
Rate	2.94 kg a.i./ha	
End-use product/formulation	IKI-3106 50 SL	
Preharvest interval	7 days	
Processed Commodity	**Average Processing Factor**	
	Cyclaniliprole	**NK-1375**
Dried prunes	3.7x	3.6x

PROCESSED FOOD AND FEED – GRAPES			**PMRA #2399203**	
Test Site	Six trials in Germany, Northern France (2 trials), Southern France, Italy and Spain			
Treatment	Broadcast foliar applications (2)			
Rate	69 - 207 g a.i./ha			
End-use product/formulation	IKI-3106 50 SL			
Preharvest interval	23 – 29 days			
Processed Commodity	**Median Processing Factor**			
	From white wine grapes		From red wine grapes	
	Cyclaniliprole	NK-1375	Cyclaniliprole	NK-1375
Filtered and pasteurized juice	0.36x	<0.17x	0.50x	<0.25x
Wet pomace	1.2x	2.3x	3.3x	4.8x

Wine at bottling	0.40x	<0.17x	<0.33x	<0.25x
Stored wine	0.36x	<0.17x	<0.36x	<0.25x
Raisins	<0.47x	0.67x	0.18x	<0.67x

LIVESTOCK FEEDING – Dairy cattle	**PMRA #2399209**

Lactating dairy cows were administered cyclaniliprole at dose levels of 0.2 ppm, 0.6 ppm and 2 ppm in the feeds for 29 – 31 consecutive days. The dose levels of 0.2, 0.6, and 2 ppm represent 1x, 3x, and 10x, respectively, the estimated more balanced diet (MBD) in dairy cattle. Matrices were analyzed for cyclaniliprole, NK-1375, NSY-27, NSY-28, and YT-1284. The residues of cyclaniliprole are presented in the table below. NSY-28 was only quantifiable in liver (highest residue: 0.032 ppm) and kidney (highest residue: 0.014 ppm) in cattle dosed at 2 ppm. The other metabolites analyzed were not quantifiable. The anticipated residues were calculated for enforcement purposes (residue definition is cyclaniliprole).

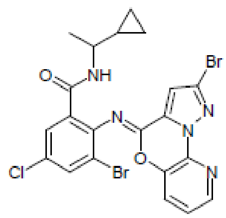
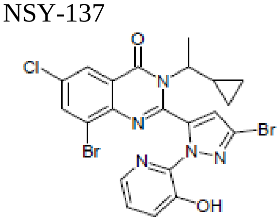
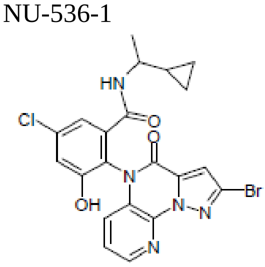
Commodity	Feeding Level (ppm)	Highest Residues (ppm)	MBD (ppm)	Anticipated Residues at MBD (ppm)
			Dairy	
Whole milk	0.2	<0.01	0.2	0.009
Skim milk		<0.01		0.01
Cream		0.015		0.011
Subcutaneous fat		<0.01		0.014
Perirenal fat		<0.01		0.015
Omental fat		<0.01		0.012
Liver		<0.01		0.014
Kidney		0.011		0.015
Muscle		<0.01		0.005
Whole milk	0.6	<0.01		
Skim milk		<0.01		
Cream		0.034		
Subcutaneous fat		0.042		
Perirenal fat		0.045		
Omental fat		0.036		
Liver		0.04		
Kidney		0.045		
Muscle		<0.01		
Whole milk	2	0.016		
Skim milk		<0.01		
Cream		0.114		
Subcutaneous fat		0.119		
Perirenal fat		0.120		
Omental fat		0.100		
Liver		0.141		
Kidney		0.114		
Muscle		0.032		

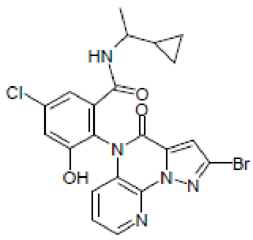
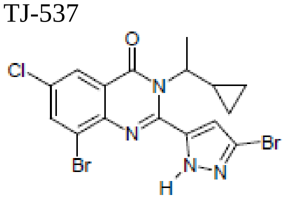
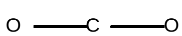
Table 7 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops: all crops** **Rotational crops: all crops**		Cyclaniliprole	
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops: all crops** **Rotational crops: all crops**		Cyclaniliprole and metabolite NK-1375	
METABOLIC PROFILE IN DIVERSE CROPS		Similar in apple, lettuce and potato.	
ANIMAL STUDIES			
ANIMALS		**Ruminant**	
RESIDUE DEFINITION FOR ENFORCEMENT		Cyclaniliprole	
RESIDUE DEFINITION FOR RISK ASSESSMENT		Cyclaniliprole and NSY-28	
METABOLIC PROFILE IN ANIMALS (goat, hen, rat)		Yes	
FAT SOLUBLE RESIDUE		Yes	
DIETARY RISK FROM FOOD AND WATER			
Basic chronic dietary exposure analysis **ADI = 0.3 mg/kg bw/day** **Estimated chronic drinking water concentration = 79 µg/L**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Alone	**Food and Water**
	All infants < 1 year	1.8	3.8
	Children 1–2 years	4.3	5.0
	Children 3 to 5 years	3.2	3.8
	Children 6–12 years	2.0	2.4
	Youth 13–19 years	1.5	1.9
	Adults 20–49 years	2.0	2.5
	Adults 50+ years	2.2	2.7
	Females 13-49 years	2.1	2.6
	Total population	2.1	2.6

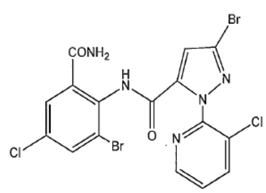
Table 8 Transformation Products of Cyclaniliprole Detected in Laboratory and Field Dissipation Studies

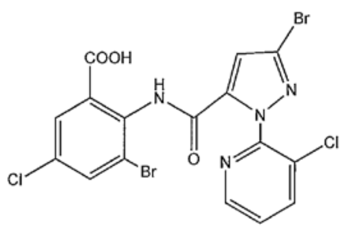
Compound	Study Type	Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
Major Transformation Products (>10% Applied Radioactivity)					
NK-1375	Soil phototransformation	42.1 (15)	42.1 (15)	Clay loam [^{14}C-Ph]	2398937
		39.9 (15)	39.9 (15)	Clay loam [^{14}C-Pz]	
	Aqueous phototransformation	39.8 (0.333)	3.4 (14)	Natural water [^{14}C-Ph]	2398872

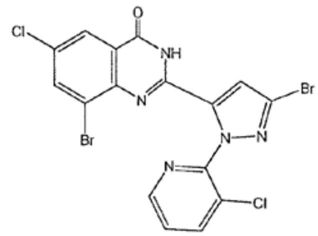
Compound	Study Type		Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
 Chemical Name: 3-bromo-2-[(2-bromo-4*H*-pyrazolo[1,5-*d*]pyrido[3,2-*b*][1,4]oxazin-4-ylidene)amino]-5-chloro-*N*-(1-cyclopropylethyl)benzamide MW: 565.65 g/mole Formula: $C_{21}H_{16}Br_2ClN_5O_2$ Water solubility: 0.07 mg/L			17.8 (0.333)	nd (14)	Natural water [^{14}C-Pz]	
			90.9 (7)	86.3 (14)	Purified water [^{14}C-Ph]	
			94.4 (2)	71.6 (14)	Purified water [^{14}C-Pz]	
	Terrestrial field dissipation	Ephrata, Washington	3.4% IMP (15)	nd (365)	300 g a.i./ha	2399218
		North Rose, New York	3.3% IMP (15)	1.5% IMP (540)	308 g a.i./ha	2399217
		Kerman, California	nd (0-545)	nd (545)	80 g a.i./ha	2399215
			3.3% IMP (30)	nd (545)	240 g a.i./ha	
		Seven Springs, North Carolina	7.7% IMP (2)	nd (540)	80 g a.i./ha	2399214
			3.9% IMP (2)	nd (540)	240 g a.i./ha	
NSY-137  Chemical Name: 8-bromo-2-[3-bromo-1-(3-hydroxypyridin-2-yl)-1*H*-pyrazol-5-yl]-6-choro-3-(1-cyclopropylethyl)quinazolin-4(3*H*)-one MW: 566 g/mole	Aqueous phototransformation		24.9 (0.75)	nd (14)	Natural water [^{14}C-Ph]	2398872
			16.1 (2)	nd (14)	Natural water [^{14}C-Pz]	
			29.5 (2)	nd (14)	Purified water [^{14}C-Ph]	
			1.2 (0.333)	nd (14)	Purified water [^{14}C-Pz]	
NU-536-1  Chemical Name: 2-[2-bromo-4-oxopyrazolo[1,5-*a*]pyrido[3,2-*e*]pyrazin-5(4*H*)-yl)-5-chloro-*N*-(1-cyclopropylethyl)-3-hydroxybenzamide MW: 504 g/mole	Aqueous phototransformation		14.2 (1.167)	4.2 (14)	Natural water [^{14}C-Ph]	2398872
			14.9 (2)	nd (14)	Natural water [^{14}C-Pz]	
			19.3 (2)	nd (14)	Purified water [^{14}C-Ph]	
			nd (14)	nd (14)	Purified water [^{14}C-Pz]	

Compound	Study Type	Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
Water solubility: 35 mg/L					
NU-536-2  Chemical Name: 2-[2-bromo-4-oxopyrazolo[1,5-*a*]pyrido[3,2-*e*]pyrazin-5(4*H*)-yl)-5-chloro-*N*-(1-cyclopropylethyl)-3-hydroxybenzamide MW: 504 g/mole Water solubility: 35 mg/L	Aqueous phototransformation	13.5 (1.167)	4.7 (14)	Natural water [^{14}C-Ph]	2398872
		16.2 (2)	nd (14)	Natural water [^{14}C-Pz]	
		18.6 (2)	nd (14)	Purified water [^{14}C-Ph]	
		4.3 (14)	4.3 (14)	Purified water [^{14}C-Pz]	
TJ-537  Chemial Name: 8-bromo-2-(3-bromo-1-*H*-pyrazol-5-yl)-6-chloro-3-(1-cyclopropylethyl)quinazolin-4(3*H*)-one MW: 473 g/mole Water solubility: 0.4 mg/L	Aqueous phototransformation	51.6 (2)	10.2 (14)	Natural water [^{14}C-Ph]	2398872
		24.4 (2)	11.7 (14)	Natural water [^{14}C-Pz]	
		6.1 (2)	nd (14)	Purified water [^{14}C-Ph]	
		nd (14)	nd (14)	Purified water [^{14}C-Pz]	
Carbon dioxide  Chemical Name: carbon dioxide MW: 44 g/mole Formula: CO_2	Soil phototransformation	7.6 (15)	7.6 (15)	Clay loam [^{14}C-Ph]	2398937
		5.4 (15)	5.4 (15)	Clay loam [^{14}C-Pz]	
	Aqueous phototransformation	8.7 (10)	7.5 (14)	Natural water [^{14}C-Ph]	2398872
		10.7 (14)	10.7 (14)	Natural water [^{14}C-Pz]	
		2.9 (10)	2.7 (14)	Purified water [^{14}C-Ph]	
		5.9 (14)	5.9 (14)	Purified water [^{14}C-Pz]	
	Biotransformation in aerobic soil (20°C)	0.6 (280)	0.6 (280)	Kenslow sandy loam [^{14}C-Ph]	2398934
		0.8 (280)	0.8 (280)	Kenslow	

Compound	Study Type	Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
				sandy loam [^{14}C-Pz]	
		0.8 (280)	0.8 (280)	Spanish clay loam [^{14}C-Ph]	
		0.6 (280)	0.6 (280)	Spanish clay loam [^{14}C-Pz]	
		1.1 (280)	1.1 (280)	Marietta sandy loam [^{14}C-Ph]	
		1.2 (280)	1.2 (280)	Marietta sandy loam [^{14}C-Pz]	
		0.8 (280)	0.8 (280)	MSL sandy clay loam [^{14}C-Ph]	
		0.4 (280)	0.4 (280)	MSL sandy clay loam [^{14}C-Pz]	
		0.4 (180)	0.4 (180)	OE sandy clay loam [^{14}C-Ph]	2398933
		0.7 (180)	0.7 (180)	OE sandy clay loam [^{14}C-Pz]	
	Biotransformation in aerobic soil (35°C)	0.7 (258)	0.7 (258)	Kenslow sandy loam [^{14}C-Ph]	2398934
		0.7 (258)	0.7 (258)	Kenslow sandy loam [^{14}C-Pz]	
		0.7 (258)	0.7 (258)	Spanish clay loam [^{14}C-Ph]	
		0.7 (258)	0.7 (258)	Spanish clay loam [^{14}C-Pz]	
		1.0 (258)	1.0 (258)	Marietta sandy loam [^{14}C-Ph]	
		1.7 (258)	1.7 (258)	Marietta sandy loam [^{14}C-Pz]	
		0.6 (258)	0.6 (258)	MSL sandy clay loam [^{14}C-Ph]	
		1.4 (258)	1.4 (258)	MSL sandy clay loam [^{14}C-Pz]	

Compound	Study Type	Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
	Biotransformation in aerobic water-sediment systems	1.0 (30)	0.2 (100)	Calwich Abbey Lake water:sandy silt loam sediment [^{14}C-Ph]	2398946
		nd (100)	nd (100)	Calwich Abbey Lake water:sandy silt loam sediment [^{14}C-Pz]	
		0.4 (59)	0.3 (100)	Swiss Lake water:sand sediment [^{14}C-Ph]	
		0.4 (100)	0.4 (100)	Swiss Lake water:sand sediment [^{14}C-Pz]	
Minor Transformation Products (<10% Applied Radioactivity)					
YT-1284  Chemical Name: 3-bromo-*N*-(2-bromo-6-carbamoyl-4-chlorophenyl)-1-(3-chloropyridin-2-yl)-1*H*-pyrazole-5-carboxamide	Biotransformation in aerobic soil (20°C)	nd (280)	nd (280)	Kenslow sandy loam [^{14}C-Ph]	2398934
		1.9 (280)	1.9 (280)	Kenslow sandy loam [^{14}C-Pz]	
		0.6 (31)	nd (280)	Spanish clay loam [^{14}C-Ph]	
		nd (280)	nd (280)	Spanish clay loam [^{14}C-Pz]	
		0.4 (31)	nd (280)	Marietta sandy loam [^{14}C-Ph]	
		nd (280)	nd (280)	Marietta sandy loam [^{14}C-Pz]	
		2.6 (280	2.6 (280)	MSL sandy clay loam [^{14}C-Ph]	
		1.4 (280)	1.4 (280)	MSL sandy clay loam [^{14}C-Pz]	
	Biotransformation in aerobic soil (35°C)	1.1 (258)	1.1 (258)	Kenslow sandy loam [^{14}C-Ph]	2398934
		1.8 (258)	1.8 (258)	Kenslow sandy loam	

Compound	Study Type	Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
				[^{14}C-Pz]	
		1.2 (258)	1.2 (258)	Spanish clay loam [^{14}C-Ph]	
		nd (258)	nd (258)	Spanish clay loam [^{14}C-Pz]	
		0.6 (258)	0.6 (258)	MSL sandy clay loam [^{14}C-Ph]	
		1.4 (258)	1.4 (258)	MSL sandy clay loam [^{14}C-Pz]	
NSY-27  Chemical Name: 3-bromo-2-[3-bromo-1-(3-chloropyridin-2-yl)- 1*H*-pyrazole-5-carboxamido]-5-chlorobenzoic acid	Biotransformation in aerobic soil	1.4 (280)	1.4 (280)	Kenslow sandy loam [^{14}C-Ph]	2398934
		0.4 (31)	nd (280)	Kenslow sandy loam [^{14}C-Pz]	
		0.4 (31)	nd (280)	Spanish clay loam [^{14}C-Ph]	
		nd (280)	nd (280)	Spanish clay loam [^{14}C-Pz]	
		0.6 (31)	nd (280)	Marietta sandy loam [^{14}C-Ph]	
		nd (280)	nd (280)	Marietta sandy loam [^{14}C-Pz]	
		nd (280)	nd (280)	MSL sandy clay loam [^{14}C-Ph]	
		nd (280)	nd (280)	MSL sandy clay loam [^{14}C-Pz]	
		1.7 (180)	1.7 (180)	OE sandy clay loam [^{14}C-Ph]	2398933
		1.0 (180)	1.0 (180)	OE sandy clay loam [^{14}C-Pz]	
NSY-28	Aqueous phototransformation	nd (14)	nd (14)	Natural water [^{14}C-Ph]	2398872
		1.6 (10)	0.9 (14)	Natural water [^{14}C-Pz]	
		nd (14)	nd (14)	Purified water [^{14}C-Ph]	
		nd (14)	nd (14)	Purified water	

Compound	Study Type	Max %AR (Sampling Interval in days)	Final %AR (Sampling Interval in days)	Comments	PMRA#
				[^{14}C-Pz]	
 Chemical Name: 8-bromo-2-[3-bromo-1-(3-chloropyridin-2-yl)-1*H*-pyrazol-5-yl]-6-chloroquinazolin-4(3*H*)-one	Biotransformation in aerobic water-sediment systems	0.8 (59)	0.7 (100)	Calwich Abbey Lake water:sandy silt loam sediment [^{14}C-Ph]	2398946
		nd (100)	nd (100)	Calwich Abbey Lake water:sandy silt loam sediment [^{14}C-Pz]	
		0.9 (100)	0.9 (100)	Swiss Lake water:sand sediment [^{14}C-Ph]	
		nd (100)	nd (100)	Swiss Lake water:sand sediment [^{14}C-Pz]	

IMP = initial measured parent
nd = not detected
OE soil = designated based on the name of the individual owning the land at the collection site
[^{14}C-Ph] = [^{14}C-phenyl] radiolabel
[^{14}C-Pz] = [^{14}C-pyrazole] radiolabel

Table 9 Fate and Behaviour of Cyclaniliprole and Transformation Products in the Environment

Property	**Test substance**	**Value**[1]	**Transformation products**	**Comments**	**PMRA#**
Abiotic transformation					
Hydrolysis	Cyclaniliprole	Effectively stable at pH 4, 7, and 9 at 50ºC	None identified	Hydrolysis is not expected to be an important route of dissipation of cyclaniliprole in the environment.	2398871
Phototransfor-mation on soil	Cyclaniliprole	DT_{50} (irradiated): 12.9 d; DT_{50} (dark): stable (SFO – combined labels) Phototransformation half-life: 25.8 d based on 12 hour light/dark cycle; equivalent to 28.3 summer days at 52°N latitude.	<u>Major, Irradiated:</u> NK-1375 <u>Minor, Irradiated:</u> CO_2	Phototransformation can contribute to the dissipation of cyclaniliprole on soil.	2398937

Property	Test substance	Value[1]	Transformation products	Comments	PMRA#
Phototransformation in water	Cyclaniliprole	Natural water: DT_{50} (irradiated): 0.459 d; DT_{50} (dark): stable (SFO – combined labels) Phototransformation half-life: 1.4 d of summer sunlight at 40°N latitude. Purified water: DT_{50} (irradiated): 0.41 d; DT_{50} (dark): stable (SFO – combined labels) Phototransformation half-life: 1.2 d of summer sunlight at 40°N latitude.	Major, Irradiated: NU-536-1 NU-536-2 NK-1375 NSY-137 TJ-537 CO_2 Minor, Irradiated: NSY-28	Can be an important route of dissipation for cyclaniliprole and its transformation products near the surface of waterbodies.	2398872
Phototransformation in air	Cyclaniliprole is not expected to be volatile under field conditions based on vapour pressure and Henry's law constant. A phototransformation study in air is not required.				
Biotransformation					
Biotransformation in aerobic soil	Cyclaniliprole	OE sandy clay loam: DT_{50}: 929 d; DT_{90}: 3907 d (DFOP – combined labels; representative half-life: 1280 d)	Minor: NSY-27 CO_2	Cyclaniliprole is persistent. Biotransformation in aerobic soil is not an important route of dissipation for cyclaniliprole.	2398933
		20°C Kenslow sandy loam: DT_{50}: 1709 d; DT_{90}: 5676 d (SFO – combined labels) Spanish clay loam: DT_{50}: 1728 d; DT_{90}: 5740 d (SFO – combined labels) Marietta sandy loam: DT_{50}: 1138 d; DT_{90}: 3782 d (SFO – combined labels) MSL sandy clay loam: DT_{50}: 1409 d; DT_{90}: 4679 d (SFO – combined labels)	Minor: YT-1284 NSY-27 CO_2	Cyclaniliprole is persistent. Biotransformation in aerobic soil is not an important route of dissipation for cyclaniliprole.	2398934
		35°C Kenslow sandy loam:	Minor: YT-1284	Cyclaniliprole is persistent.	

Property	Test substance	Value[1]	Transformation products	Comments	PMRA#
		DT_{50}: 638 d; DT_{90}: 2119 d (SFO – combined labels) Spanish clay loam: DT_{50}: 588 d; DT_{90}: 1953 d (SFO – combined labels) Marietta sandy loam: DT_{50}: 548 d; DT_{90}: 1820 d (SFO – combined labels) MSL sandy clay loam: DT_{50}: 681 d; DT_{90}: 2262 d (SFO – combined labels)	CO_2	Biotransformation in aerobic soil is not an important route of dissipation for cyclaniliprole.	
Biotransformation in anaerobic soil	Cyclaniliprole	OE sandy clay loam: DT_{50}: 610 d; DT_{90}: 2027 d (SFO – combined labels)	Minor: Unidentified product CO_2	Cyclaniliprole is persistent. Biotransformation in anaerobic soil is not an important route of dissipation for cyclaniliprole.	2398936
Biotransformation in aerobic water-sediment systems	Cyclaniliprole	Calwich Abbey Lake water:sandy silt loam sediment: Total system DT_{50}: 694 d; DT_{90}: 2306 d (SFO – combined labels) Swiss Lake water:sand sediment: Total system DT_{50}: 495 d; DT_{90}: 1645 d (SFO – combined labels)	Minor: NSY-28 CO_2	Cyclaniliprole is persistent. Biotransformation is not an important route of dissipation for cyclaniliprole in aerobic water-sediment systems.	2398946
Biotransformation in anaerobic water-sediment systems	Cyclaniliprole	Calwich Abbey Lake water:sandy silt loam sediment: Total system DT_{50}: 854 d; DT_{90}: 2837 d (SFO – combined labels) Swiss Lake water:sand sediment: Total system DT_{50}: 794 d; DT_{90}: 2637 d (SFO – combined labels)	Minor: ‘Metabolite A’ CO_2	Cyclaniliprole is persistent. Biotransformation is not an important route of dissipation for cyclaniliprole in anaerobic water-sediment systems.	2398945

Property	Test substance	Value[1]	Transformation products	Comments	PMRA#
Mobility					
Adsorption / desorption in soil	Cyclaniliprole	Calke sandy loam: K_F: 7.4 L/kg; K_{FOC}: 247 L/kg; 1/n: 1.00; K_d: 7.6 L/kg; K_{OC}: 254 L/kg Beely Moor loamy sand: K_F: 79.2 L/kg; K_{FOC}: 1131 L/kg; 1/n: 1.00; K_d: 76.1 L/kg; K_{OC}: 1087 L/kg Cuckney sand: K_F: 2.8 L/kg; K_{FOC}: 567 L/kg; 1/n: 0.98; K_d: 3.0 L/kg; K_{OC}: 603 L/kg Warsop loamy sand: K_F: 6.9 L/kg; K_{FOC}: 862 L/kg; 1/n: 1.00; K_d: 6.8 L/kg; K_{OC}: 853 L/kg Biodynamic Garden sandy loam: K_F: 31.4 L/kg; K_{FOC}: 628 L/kg; 1/n: 0.98; K_d: 33.4 L/kg; K_{OC}: 669 L/kg	Not applicable	Cyclaniliprole is classified as having low to moderate potential for mobility in soil.	2398941
	NK-1375	K_{OC}: 25119 L/kg, estimated by High Performance Liquid Chromatography		Transformation product NK-1375 is expected to be immobile in soil.	2398943
Soil leaching	Not required as an acceptable adsorption/desorption study was submitted.				
Volatilization	Not required based on the low vapour pressure (2.4×10^{-6} Pa at 25°C) and Henry's law constant (9.5×10^{-8} atm m^3/mole at 20°C).				
Field studies					
Field dissipation	Cyclaniliprole 50SL (End-Use Product)	Ephrata, Washington: DT_{50}: 1247 d; DT_{90}: 4141 d (SFO) Carry-over to the next growing season (Day 365): 91% initial measured parent	Minor: NK-1375 Deepest layer with detections: 0-7.6 cm	Leaching may be an important route of dissipation for cyclaniliprole. Cyclaniliprole has the potential to accumulate in soil and carry over to	2399218

Property	Test substance	Value[1]	Transformation products	Comments	PMRA#
		Residues at study termination (Day 540) were 61.2% of initial measured levels. Deepest layer with detections: 91.4-106.7 cm		the next growing season.	
		<u>North Rose, New York:</u> DT_{50}: 155 d; DT_{90}: 1040 d Representative field DT_{50} (DFOP; slow $t_{1/2}$): 381 d; excludes outliers for Days 420 and 480 Carry-over to the next growing season (Day 365): 31.8% initial measured parent Residues at study termination (Day 540) were 32.6% of initial measured levels. Deepest layer with detections: 15.2-30.5 cm	<u>Minor:</u> NK-1375 Deepest layer with detections: 0-7.6 cm	Cyclaniliprole has the potential to accumulate in soil and carry over to the next growing season.	2399217
	Cyclaniliprole 100L (End-Use Product)	<u>Kerman, California:</u> 80 g a.i./ha DT_{50}: 494 d; DT_{90}: 2444 d Representative field DT_{50} (DFOP; slow $t_{1/2}$): 840 d 240 g a.i./ha DT_{50}: 743 d; DT_{90}: 2470 d (SFO) Carry-over to the next growing season (Day 241): 62.4-65.2% initial measured parent Residues at study termination (Day 545): 41.1-50.3% of initial measured levels. Deepest layer with detections: 61-76.2 cm	<u>Minor:</u> NK-1375 Deepest layer with detections: 0-7.6 cm	This site is not in an ecoregion representative of Canadian conditions. Results from this study are supplemental to those from sites in Washington and New York. Leaching may be an important route of dissipation for cyclaniliprole. Cyclaniliprole has the potential to accumulate in soil and carry over to the next growing season.	2399215

Property	Test substance	Value[1]	Transformation products	Comments	PMRA#
		Seven Springs, North Carolina: 80 g a.i./ha DT_{50}: 7.46 d; DT_{90}: 997 d Representative field DT_{50} (DFOP; slow $t_{1/2}$): 485 d 240 g a.i./ha DT_{50}: 34.5 d; DT_{90}: 1050 d Representative field DT_{50} (DFOP; slow $t_{1/2}$): 477 d Carry-over to the next growing season (Day 243): 24.8-42.4% initial measured parent Residues at study termination (Day 544): 26.6-27% of initial measured levels. Deepest layer with detections: 15.2-30.5 cm	Minor: NK-1375 Deepest layer with detections: 0-7.6 cm	This site is not in an ecoregion representative of Canadian conditions. Results from this study are supplemental to those from sites in Washington and New York. Cyclaniliprole has the potential to accumulate in soil and carry over to the next growing season.	2399214
Aquatic field dissipation	No aquatic field dissipation study with cyclaniliprole was submitted, and data on the aquatic field disspiation of cyclaniliprole are not required.				
Bioconcentration/bioaccumulation					
Bioconcentra-tion in fish	Cyclaniliprole	Whole body steady state BCF: 48-95 Whole fish steady state BCF normalised to 5% lipid content: 193-374 Whole body kinetic BCF: 87.8-202 Time to 95% depuration of 14-C-residues: 96-120 d for whole fish	Minor metabolites: YT-1284 NK-1375 Up to six unidentified metabolites	Cyclaniliprole did not bioconcentrate in large amounts in fish under the test conditions of the study. Clearance time to 95% depuration of ^{14}C-residues was 96 to 120 days.	2398975

[1] Kinetics models: SFO = single first-order; DFOP = double first-order in parallel
OE soil = designated based on the name of the individual owning the land at the collection site

Table 10 Toxicity of Cyclaniliprole, the Transformation Product NK-1375 and the End-use Product Cyclaniliprole 50SL Insecticide to Non-target Terrestrial Species

Organism	**Exposure**	**Test substance**	**Endpoint value**	**Degree of toxicity[1]**	**PMRA#**
Invertebrates					
Earthworm, *Eisenia fetida*	14-d Acute	Cyclaniliprole	LC_{50} > 1000 mg a.i./kg dry soil (nominal) NOEC = 1000 mg a.i./kg dry soil (nominal; highest concentration tested)	No classification	2398997
	14-d Acute	Cyclaniliprole 50SL (End-Use Product)	LC_{50} > 1000 mg product/ kg dry soil (> 46.3 mg a.i./kg dry soil) NOEC = 1000 mg product/kg dry soil (46.3 mg a.i./kg dry soil; highest concentration tested)	No classification The end-use product is not more toxic than cyclaniliprole alone.	2399081
	56-d Reproduction; 28-d adult exposure and an extra 28-d exposure for cocoons/ juveniles	Cyclaniliprole	NOEC = 1000 mg a.i./kg dry soil (nominal; highest concentration tested)	No classification	2398999
Collembola, *Folsomia candida*	28-d Reproduction, artificial soil	Cyclaniliprole	$NOEC_{mortality}$ = 5 mg a.i./kg dry soil (nominal) (68% mortality at 10 mg a.i./kg dry soil) $EC_{50\ fecundity}$ = 6.76 mg a.i./kg dry soil (nominal) $NOEC_{fecundity}$ = 2.5 mg a.i./kg dry soil (nominal)	No classification	2398993
Predatory soil mite, *Hypoaspis aculeifer*	14-d Reproduction, artificial soil	Cyclaniliprole	LC_{50} > 1000 mg a.i./kg dry soil $EC_{50\ fecundity}$ > 1000 mg a.i./kg dry soil $NOEC_{fecundity}$ = 555.56 mg a.i./kg dry soil	No classification	2398995

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Honey bee, *Apis mellifera*	96-h Oral, adults	Cyclaniliprole	LD_{50} = 0.702 µg a.i./bee Behavioural abnormalities (e.g., apathy) were observed in all dose groups except for the lowest group, but these decreased over time.	Highly toxic	2398991
	96-h Oral, adults	Cyclaniliprole 50SL (End-Use Product)	LD_{50} = 4.31 µg product/bee (0.200 µg a.i./bee) Behavioural abnormalities (e.g., apathy and/or moving co-ordination problems) were observed in all dose groups except for the lowest group, but these decreased over time.	Highly toxic (based on TGAI)	2399053
	96-h Contact, adults	Cyclaniliprole	LD_{50} = 0.952 µg a.i./bee Behavioural abnormalities (e.g., apathy or/and moving coordination problems) were found throughout the experiment in all dose groups except the lowest test group.	Highly toxic	2398991
	96-h Contact, adults	Cyclaniliprole 50SL (End-Use Product)	LD_{50} = 10.9 µg product/bee (0.507 µg a.i./bee) Behavioural abnormalities (e.g., apathy, moving co-ordination problems and/or cramping) were observed throughout the experiment.	Highly toxic (based on the technical grade active ingredient)	2399053
	10-d Chronic, adults	Cyclaniliprole 50SL (End-Use Product)	NOAED = 0.49 µg product/bee/day (0.023 µg a.i./bee/day)	No classification	2612298

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			(mortality) Discoordinated movements and/or apathy were observed at doses of 0.64 mg a.i./kg feeding solution (0.023 µg a.i./bee/day) and above.		
	72-h Oral, single exposure, larvae	Cyclaniliprole	LD_{50} = 0.16 µg a.i./larva/day	No classification	2612300
	21-d Oral, repeated exposure, larvae	Cyclaniliprole	NOAED = 0.0649 µg a.i./larva/day (emergence)	No classification	2718601
	Foliage residue toxicity (80 g a.i./ha on alfalfa)	Cyclaniliprole 50SL (End-Use Product)	RT_{25} < 3 hours (<1% mortality)	No classification Limited mortality observed from dried residues on leaves.	2663361
Predatory mite, *Typhlodromus pyri*	7-d Glass plates (screening level)	Cyclaniliprole 50SL (End-Use Product)	LR_{50} = 105 g a.i./ha $ER_{50\ fecundity}$ = 125 g a.i./ha	No classification	2399075
Parasitoid wasp, *Aphidius rhopalosiphi*	48-h Glass plates (screening level)	Cyclaniliprole 50SL (End-Use Product)	LR_{50} = 0.507 g a.i./ha $ER_{50\ fecundity}$ = 0.021 g a.i./ha	No classification	2399076
	48-h Extended laboratory/aged residues; exposure to residues and aged residues on plant leaves	Cyclaniliprole 50SL (End-Use Product)	0 DAT[2]: LR_{50} = 4.32 g a.i./ha $ER_{50\ fecundity}$ = 4.09 g a.i./ha 14 DAT: LR_{50} = 24.1 g a.i./ha $ER_{50\ fecundity}$ = 12.68 g a.i./ha 28 DAT: LR_{50} > 80 g a.i./ha $ER_{50\ fecundity}$ = 47.74 g a.i./ha 56 DAT: LR_{50} > 80 g a.i./ha $ER_{50\ fecundity}$ > 80 g a.i./ha	No classification	2399077
Ladybird beetle, *Coccinella septempunctata*	Extended laboratory/aged residues; exposure to	Cyclaniliprole 50SL (End-Use Product)	0 DAT[2]: Pre-imaginal LR_{50} = 28.1 g a.i./ha	No classification	2399079

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
	residues and aged residues on plant leaves; 3 to 4-d old larvae were exposed until adult emergence		$ER_{50\ fecundity}$ > 27.2 g a.i./ha (highest rate tested due to to mortality of 1st generation larvae at higher rates) 28 DAT and 56 DAT: Pre-imaginal LR_{50} > 80 g a.i./ha $ER_{50\ fecundity}$ > 80 g a.i./ha (highest rate tested)		
Rove beetle, *Aleochara bilineata*	Extended laboratory/aged residues; exposure to residues and aged residues on artificial soil 28-d adult exposure and an extra 7 d for pupae/fecundity assessment	Cyclaniliprole 50SL (End-Use Product)	0 DAT[2]: LR_{50} = 84.3 g a.i./ha $ER_{50\ fecundity}$ > 80 g a.i./ha (31% reduction in fecundity) 14 DAT, 28 DAT and 56 DAT: LR_{50} > 80 g a.i./ha $ER_{50\ fecundity}$ > 80 g a.i./ha	No classification	2399078
Birds					
Bobwhite quail, *Colinus virginianus*	Acute oral	Cyclaniliprole	LD_{50} > 2000 mg a.i./kg bw NOEL = 2000 mg a.i./kg bw (highest dose tested)	Practically non-toxic	2398950
	5-d Dietary	Cyclaniliprole	LC_{50} > 5000 mg a.i./kg diet (LD_{50} > 1000 mg a.i./kg bw/d) NOEC = 5000 mg a.i./kg diet (highest concentration tested) (NOEL = 1000 mg a.i./kg bw/d)	Practically non-toxic	2398954
	22-week Reproduction	Cyclaniliprole	NOEC = 100 mg a.i./kg diet (eggshell thickness, viable embryos of eggs set, live 3-week embryos as a proportion of those viable, normal hatchlings of viable	No classification	2398958

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			embryos and of live 3-week embryos, 14-day survivors of eggs laid, and chick bodyweights at 14 days) (NOEL = 9.1 and 8.8 mg a.i./kg bw/d for males and females, respectively; LOEL = 26.9 and 25.7 mg a.i./kg bw/d for males and females, respectively)		
Mallard duck, *Anas platyrhynchos*	5-d Dietary	Cyclaniliprole	LC_{50} > 5000 mg a.i./kg diet (LD_{50} > 1633 mg a.i./kg bw/d) NOEC = 5000 mg a.i./kg diet (highest concentration tested) (NOEL = 1633 mg a.i./kg bw/d)	Practically non-toxic	2398956
	23-week Reproduction	Cyclaniliprole	NOEC = 60 mg a.i./kg diet (highest concentration tested) (NOEL = 8 mg a.i./kg bw/d for males and 9 mg a.i./kg bw/d for females)	No classification	2398960
Canary, *Serinus canaria*	Acute oral	Cyclaniliprole	LD_{50} > 2000 mg a.i./kg bw NOEL = 2000 mg a.i./kg bw (highest dose tested)	Practically non-toxic	2398952
Mammals					
Rat	Acute oral	Cyclaniliprole	LD_{50} > 2000 mg a.i./kg bw	Practically non-toxic	2398885
	Acute oral	NK-1375	LD_{50} > 2000 mg/kg bw	Practically non-toxic	2398886
	Acute oral	Cyclaniliprole 50SL Insecticide (End-Use Product)	LD_{50} > 2000 mg product/kg bw (> 92.6 mg a.i./kg bw)	Formulation is practically non-toxic	2399177
	2-generation Reproduction, exposure through the diet	Cyclaniliprole	NOAEC = 20000 mg a.i./kg diet (highest concentration tested) ($NOAEL_{\text{parental and}}$	No classification	2398916, 2398919

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
			reproductive toxicity = 1046 and 1589 mg a.i./kg bw/d for males and females, respectively; NOAEL offspring toxicity = 1589 mg a.i./kg bw/d)		
Vascular plants					
Monocot and dicot crop species (cabbage, carrot, cucumber, lettuce, soybean, tomato, corn, oat, onion and perennial ryegrass)	21-d Seedling emergence	Cyclaniliprole 50SL (End-Use Product)	ER_{25} > 1000 g a.i./ha for all species tested	No classification	2399082
Monocot and dicot crop species (cabbage, carrot, cucumber, lettuce, soybean, tomato, corn, oat, onion and perennial ryegrass)	21-d Vegetative vigour	Cyclaniliprole 50SL (End-Use Product)	ER_{25} > 1000 g a.i./ha for all species tested	No classification	2399083

[1] Atkins *et al*.(1981) for bees and U.S. EPA classification for others, where applicable
[2] DAT = days after treatment before exposure

Table 11 Effects of the End-use Product Cyclaniliprole 50SL Insecticide on Honey Bees based on Tier II (Semi-field) and Tier III (Field) Studies

Study design	Conclusion	Uncertainties	PMRA #
Tier II (semi-field)			
Study type: Semi-field study Rate: 80 g a.i./ha Replicate: Four hives per one tunnel Colony size before exposure: 12688 bees in the control and 15113 bees in the test item and 12275 bees in the reference control Product applied:	Adult mortality: As compared to the control, exposure to the test item treatment resulted in significantly increased in-hive worker mortality and forager mortality during the overall exposure phase. However, it is noted that pre-exposure mortality was higher in many cases than the exposure phase. Mean adult mortality before exposure was 11.5, 17.7 and 29 dead bees/colony/day in the control, treatment hives and reference control hives, respectively. From DAT 0 to 8, corresponding mortality was 8.6, 16.9 and 14.7 dead bees/colony/day; and	Timing of observations for mortality occurred prior to exposure instead of post-exposure for two out of the three observation periods. Control hives exhibited poor performance (particularly for brood development) throughout the course of the study, which made a comparison difficult. In some cases, control hives performed more poorly than the reference item hives. There was also a deviation from protocol regarding the number	2524490

Study design	Conclusion	Uncertainties	PMRA #
Cyclaniliprole 50SL (End-Use Product) Application timing: Applied in the morning before bee foraging activity Reference item and rate: Fenoxycarb at 300 g a.i./ha Crop: *Phacelia tanacetifolia* Tunnel size: 99 m^2 Location: Switzerland Year: 2014 Exposure length: Colonies were in tunnels for 15 days (6-day acclimation period and 9 days of treatment). Following treatment (DAT 9 to 29), bees were moved to a monitoring site. Observations/ endpoints: Hives were observed for mortality, foraging activity, behavioural abnormalities, condition, bee brood development, brood termination rate, brood index, and brood compensation index. Residue collection: none	from DAT 9 to 29, corresponding mortality was 16.7 dead bees/colony/day (in the control), 21.5 dead bees/colony/day (in the treatment hives), and 24.2 dead bees/colony/day (in the reference control hives). Forager mortality (on sheets in tunnels) was 15.3, 27.8 and 13.7 dead bees/colony/day in the control, treatment and reference control tunnels, respectively. Brood and colony condition: When compared to the control, there were no adverse effects of the test item treatment on brood termination rates (the percent of eggs which failed to develop to adult emergence) of initially selected eggs or on performances of the brood index (based on the number of each brood stage at each assessment period). Also, there were no treatment-related effects on the brood compensation index (the ability to recover from previous brood loss) over an entire brood cycle, when compared to the control. However, it is noted that brood development in the control was reduced. As compared to the control, the performance of overall colony strength in the test item treatment was significantly decreased in the short-term (at the end of the tunnel phase, DAT 8) and in the medium-term (at the end of the monitoring phase, DAT 29). Strength on DAT 8 was +46.4, +14.5 and +4.2% in the control hive, treatment hive and treatment control hive, respectively. Corresponding strength on DAT 29 was +7.3, -32 and -21.1%. Furthermore, as compared to the control, the performance of overall brood investment and/or development (i.e., brood nest size, including eggs, larvae and pupae) in the test item treatment was significantly decreased in the medium-term (at the end of the monitoring phase, DAT 29). In-hive worker and pupal mortality was significantly increased during the	eggs selected for the study, because less than 300 eggs were available from one replicate of the control and two treatment replicates. This may have resulted in ‘weaker’ hives at study initiation. Symptoms of poisoning were not defined. Behavioural abnormality was listed as aggressiveness, intensive flying activity without landing on the crop, clustering in the hive entrance, and intoxication symptoms. Poor weather conditions led to a decrease in foraging and potential effects to the colony. It is unknown if confinement also led to poor colony development over the course of the study. Owing to the poor weather conditions, supplemental sugar solution was also offered to the hives, which may have diluted exposure. Land description at the monitoring site was lacking and it is unknown if bees were additionally exposed to other chemicals. The application rate in the study (80 g a.i./ha) was equal to the maximum proposed single application rate in Canada; however, it was lower than the proposal maximum annual rate (300 g a.i./ha). Residues were not collected in this study to confirm exposure.	

Study design	Conclusion	Uncertainties	PMRA #
	overall post-exposure phase (DAT 9 to 29) at the monitoring site. Symptoms of poisoning were observed in bees at the entrances of the hives in the test item treatment during the first four days after application. Mean pupal mortality in the control from DAT 0 to 8 and DAT 9 to 29 ranged from 0.4 to 1.7 dead bees/colony/day, compared to 1.1 to 2.8 dead bees/colony/day in the treatment hives and 1.9 to 8.2 dead bees/colony/day in treatment control hives. Foraging activity: After the test item application, a significant decrease of foraging activity (mostly on the first day of application) in the test item treatment was detected in comparison to the control. This was accompanied by observations of abnormal behaviour (e.g., aggressiveness), such as symptoms of poisoning. **Summary:** **In conclusion, Cyclaniliprole 50SL, applied during the early morning prior to bee flight activity at a rate of 80 g a.i. cyclaniliprole per hectare resulted in adverse effects that could not be ruled out as treatment-related. These included an increase in in-hive and forager adult and pupal mortality during exposure, a decrease in colony strength compared to the control, and a decrease in brood nest size after the exposure and observation period concluded 29 DAT. Foraging activity decreased significantly one day after application. These results are uncertain because mortality in the control and treated hives was higher during pre-treatment and brood development in the control was reduced during the experiment.**		

Study design	Conclusion	Uncertainties	PMRA #
Study type: Semi-field study Rate: 40 g a.i./ha Replicates: 4 tunnels (3 for biological assessment and 1 residue monitoring) with 1 colony per tunnel Colony size before exposure: 7432 bees in the control and 6500 bees in the test item and 6522 bees in the reference control Product applied: Cyclaniliprole 50SL (End-Use Product) Reference chemical and rate: Fenoxycarb at 250 g/kg Crop: *Phacelia tanacetifolia* Application timing: Applied during bloom in the evening after bee flight Exposure duration: Colonies were in tunnels for 7 days of treatment. Following treatment (DAT 8 to 28), bees were moved to a monitoring site. Tunnel size: 132 m^2 Location: Spain Year: 2013 Observation/ endpoints: Hives were observed for mortality, foraging activity, behavioural abnormalities, condition, bee brood development,	Adult mortality: There was no significant difference in mean mortality between the control, treatment and reference control hives. Before application, mortality appeared higher in all hives and ranged from 117.3 to 144.9 dead bees per colony per day. During the exposure period, mean mortality ranged from 70.3 to 85.2 dead bees per colony. However, it is noted by the reviewer that on day 0aa there was a trend of higher mortality in the treatment hives (116 dead bees) compared to the control (47 dead bees) and reference control (47 dead bees). The reference control, fenoxycarb, is expected to exert effects on larvae, not adults. Mean mortality during the post exposure phase (DAT 8 to 28) was 12.1, 3.1 and 9.4 dead bees in the control, treatment hive and reference control, respectively. Brood and colony condition: There was no significant difference for control, treatment or reference control hives. Pupal mortality was similar and low over the course of the study (0.1 to 1.8 dead pupae per colony) in all hives (control, treatment and reference control). Overall mean pupal mortality in the reference control was significantly higher than the control and treatment hives. Mean dead pupae from day 0 to 28 (after application) was 0.1, 0.4 and 1.8 in the control, treatment hives and reference control hives, respectively. Colony strength appeared to decline in both the control and treatment hives over the course of the study when compared to pre-treatment levels (from a range of 88 to 99% on DAT 3 (6565, 6457 and 6695 bees in the control, treatment and reference control hives, respectively), to a range of 66 to 69 % (4940, 4463 and 7095 bees in the control, treatment and reference control hives, respectively)	Brood termination rate of the control, with a mean of 53.5%, appears to be high; although it is noted that the termination rate in the reference control was higher (88.8%). Mean adult mortality ranged between 70.3 and 85.2 dead bees/colony/day in the control, treatment hives and reference hives (treated with fenoxycarb, which is more toxic to larvae than adults). The application rate in the study (40 g a.i./ha) is below the proposed maximum single application rate (80 g a.i./ha) and maximum annual rate (300 g a.i./ha). Colony strength of the control and treatment groups decreased to 66% and 69% of the initial strength, respectively, by DAT 26, indicating that colony health was reduced during the course of the study by some non-treatment-related factors. Mean adult mortality before application in the treatment and reference control hives and the control ranged from 117 to 144.9 dead bees/colony from DAT -3 to DAT -1), which appears high. Control and reference bees were sprayed while foraging, while the treatment hives were sprayed after foraging. Fenoxycarb was used as the control reference, which is expected to exert toxic effects on larvae, not adults. Residues were detected in the treatment hives, which indicated that exposure did occur.	2399068

Study design	Conclusion	Uncertainties	PMRA #
and brood termination rate. <u>Residue collection:</u> Residues in nectar combs, honey stomachs and pollen combs, pollen from traps, pollen from bees and flowers were collected.	on DAT 26). Comparatively, the colony strength in the reference control was over 100% during the study. Therefore, there may have been some issues with the performance of the control and treatment hives, which was not related to Cyclaniliprole 50SL. <u>Foraging:</u> There was similar foraging among all hives before application (DAT -3 to -1) (15.3, 12.9 and 14.7 bees/m^2/tunnel in the control, treatment, and reference control, respectively). Prior to application on day 0, foraging was slightly lower in the treatment hives (8.8 bees/m^2/tunnel) compared to 13.4 in the control and 24.1 bees/m^2/tunnel in the reference control. From DAT 1 to 7, foraging was 17.9, 20.1 and 14.6 bees/m^2/tunnel in the control, treatment and reference control hives, respectively. **<u>Summary:</u>** **Overall, no adverse effects on mean adult survival, pupae survival, foraging activity, colony strength, conditions of the colony performance and brood development were observed. It is noted that although the mean adult mortality was similar between all hives, the mean mortality just after application (DAT 0aa) was 47, 116 and 47 dead bees in the control, treatment and reference control hives, respectively, indicating a higher trend of dead bees just after application in the hives treated with Cyclaniliprole 50SL that was transient and returned to levels similar to control after 1 day. The following day, mortality in all hives was similar (between 26 and 33 dead bees in the control and treatment hives). The brood termination rate in the control was up to 53.5% (which was higher than the treatment hives) but lower than the reference control hives (which had**		

Study design	Conclusion	Uncertainties	PMRA #
	88.8% brood termination rate). However, the colony strength of the control and treatment groups decreased to 66% and 69% of the initial strength, respectively, by DAT 26, indicating that colony strength was reduced during the course of the study by some non-treatment-related factors. Residues and exposure: The residues of Cyclaniliprole 50SL found in pollen and flowers indicate exposure of the honey bees to the residues of the test item. Residues were not detected in nectar samples. In treatment hives, residues in pollen combs ranged from 0.109 to 0.238 mg/kg, residues in pollen traps were 1.344 mg/kg, residues in pollen from bees ranged from < LOQ (0.005 mg/kg) to 0.496 mg/kg and residues in flowers ranged from 0.790 to 1.463 mg/kg. There were no residues in control hives or plants.		
Study type: Semi-field study Rate: 40 g a.i./ha × 2 Replicates: 4 tunnels (3 for biological assessment and 1 residue monitoring) with 1 colony per tunnel Colony size before exposure: 5985 bees in the control and 4740 bees in the test item and 5550 bees in the reference control Product applied: Cyclaniliprole 50SL (End-Use Product) Reference chemical and rate: Fenoxycarb at 250 g/kg Crop: *Phacelia tanacetifolia*	Adult mortality: There was no significant difference in mean mortality between the hives over the course of the study. Mortality was consistently higher in the control and reference control compared to the treatment hives. Mean mortality after the first application and before the second application was 92.2, 57.6 and 101.7 dead bees/colony/day in the control, treatment hive and reference control hive, respectively. On the day of application (day 0aa (after application)) following exposure, mean mortality was 97.7, 157.3 and 69 dead bees/colony in the control, treatment and reference control hives, respectively. Although not statistically significant, there was a trend of higher mortality in the treatment hives. Mean mortality during the exposure phase was 128, 71.8 and 18.9 dead bees/colony/day in the control, treatment and reference control hives, respectively. Brood and colony condition:	The application rate in the study (40 g a.i./ha applied twice) is below the proposed maximum single application rate (80 g a.i./ha) and maximum annual rate (300 g a.i./ha). Fenoxycarb was used as the control reference, which is expected to exert toxic effects on larvae, not adults. Control and reference bees were sprayed while foraging, while the treatment hives were sprayed when bees were not present. Some residues of cyclaniliprole were found in the control hives. There was only 2 metres between tunnels, and therefore, it is possible that cyclaniliprole drifted to the control tunnels. On DAST 14 (19-07-2013) after the daytime application each honey bee colony was fed with	2399073

Study design	Conclusion	Uncertainties	PMRA #
Application timing: The first application was made during bloom with no bees present and the second application was made 15 days later during bloom after bee activity (in the evening). Location: Germany Year: 2013 Exposure duration: Colonies were in tunnels for 7 days of treatment. Following treatment (DAT 8 to 28), bees were moved to a monitoring site. Tunnel size: 80 m^2 Observations/ endpoints: Hives were observed for mortality, foraging activity, behavioural abnormalities, condition, bee brood development, and brood termination rate. Residue collection: Residues in nectar combs, honey stomachs and pollen combs, pollen from traps, pollen from bees and flowers were collected.	Mean pupal mortality during the study was similar and low between the control and treatment hives (0 to 0.4 dead pupae/tunnel/day). In comparison, pupal mortality was significantly higher in the reference toxicant (up to 23 dead pupae/tunel/day during the study following application). The mean brood termination rate was 38.8, 43.2 and 94.3% in the control, treatment hives and reference toxicant, respectively. Colony strength was 5985, 4740 and 5550 bees/colony before treatment in the control treatment, and reference hives. On DAST 26, the corresponding mean colony strength was 7965, 5880 and 4665 bees/colony. Strength increased in all hives (by 33, 24 and 15.9% in the control, treatment and reference hives, respectively). Foraging: There was similar foraging between hives prior to application (5.1 to 7.3 bees/m^2/colony/day). During the exposure phase, mean foraging was also similar with a range of 14.4 to 17.7 bees/m^2/colony/day among all hives. However, on day 1 (after application) foraging was statistically lower in the treatment hives (13.6 bees/ m^2) compared to the control (17.1 bees/ m^2). Foraging was also lower on day 2 (20 and 30.7 bees/m^2 in the treatment and control hives respectively). By day 3, foraging was similar in the control and treatment hives (19.4 and 21.7 bees/m^2, respectively). There was no statistical difference observed between the control and the reference hives. **Summary:** **Overall, no adverse treatment-related effects on adult and pupae mean mortality, colony strength, conditions of the colony performance and brood**	1.5 L ApiGold Bee feeding syrup. This may have resulted in a diluted exposure. Although not statistically significant, there was higher mortality in the treatment hives on the day of application (following treatment, DAT 0aa). Variability in the data may have resulted in lower statistical sensitivity. During the exposure phase, control adult mean mortality reached up to 247 dead bees, and reference item adult mean mortality reached up to 270 dead bees. This appears to be high (to the reviewer).	

Study design	Conclusion	Uncertainties	PMRA #
	development were observed. Adult mortality was consistently higher in the control and reference control compared to the treatment hives, except on the day of application. On the day of application (day 0aa) following exposure mean mortality was 97.7, 157.3 and 69 dead bees/colony in the control, treatment and reference control hives, respectively (which indicated a trend of higher mortality which was not statistically significant, transient, and returned to levels similar to control after 1 day). The following day, mortality in all hives was similar (between 26 and 29 dead bees). **There was a statistically significantly decrease of foraging activity on DAST 0 and DAST 1 after the 2nd test item treatment application which was only temporary and is attributed by the study author to the generally lower foraging activity in the test item group before test item application rather than a treatment effect.** Residues and exposure: The residues of Cyclaniliprole 50SL found in pollen and flowers indicate exposure of the honey bees to the residues of the test item. No residues were detected in nectar. Residues in pollen from combs at the treatment hives were 0.038 mg/kg, and residues in pollen from traps ranged from 0.023 to 0.311 mg/kg. Pollen from bees ranged from < LOQ (0.005 mg/kg) to 0.276 mg/kg and pollen from flowers ranged from 0.386 to 1.754 mg/kg. In the control hives, residues in pollen from bees were found up to 0.089 mg/kg.		
Study type: Semi-field study Application rate: 53.32 g a.i./ha Replicates: 4 tunnels (3	Adult mortality: There was no significant difference in mean mortality between the hives over the course of the study. Before application (DAT -3 to -1ba (before application)), mean mortality was	The application rate in the study (53.32 g a.i./ha applied once) is below the proposed maximum single application rate (80 g a.i./ha) and maximum annual rate (300 g a.i./ha). It is above the maximum proposed	2399070

Study design	Conclusion	Uncertainties	PMRA #
for biological assessment and 1 residue monitoring) with 1 colony per tunnel Colony size before exposure: 3525 bees in the control, 4170 bees in the test item, and 3255 bees in the reference control Product applied: Cyclaniliprole 50SL (End-Use Product) Reference chemical and rate: Fenoxycarb at 250 g/kg Crop: *Phacelia tanacetifolia* Application timing: Application was made during bloom after bee activity (in the evening). Exposure period: Colonies were in tunnels for 7 days of treatment. Following treatment (DAT 8 to 28), bees were moved to a monitoring site. Tunnel size: 80 m^2 Location: Germany Year: 2014 Observation/ endpoints: Hives were observed for mortality, foraging activity, behavioural abnormalities, condition, bee brood development, and brood termination rate. Residues collected: Residues in nectar combs, honey stomachs and pollen combs, pollen from traps, pollen from bees	68.2, 74.1 and 87.9 dead bees per colony/day in the control, treatment and reference control hives, respectively. The corresponding mortality on day 0aa (after application), was 60.3, 108 and 46.7. Although not statistically significant, there was a trend of higher mortality in the treatment hives just after application. By day 1, mortality was low and similar among all hives. During the exposure phase the mean mortality was similar among all hives (range of 40.9 to 45.4 dead bees/colony/day). Following exposure, mean mortality was also similar (range of 13.9 to 18.1 dead bees/colony/day). Brood and colony condition: There was no significant difference in mean pupal mortality during the study among hives (range of 0.5 to 1.3 dead larvae/colony/day). Brood termination rates were also similar among all hives (range of 38.7 to 51.7% on day 21), indicating a lack of sensitivity of the reference control. Colony strength was also similar among all hives, and increased by study termination (range of 190 to 222% increase by day 27). Foraging: Mean foraging activity was similar among hives before exposure (DAT -3 to -1 ba) and the first day of exposure (DAT 0aa) (range of 10.6 to 11.9 bees per m^2/colony). From day 2 onward, when it was raining, the foraging activity declined in all hives from day 2 to 7. The overall mean foraging from day 0 to 7aa was 4.5, 2.8 and 4.1 bees per m^2/colony in the control, treatment and reference control hives, respectively. **Summary:** **Overall, no adverse treatment-related effects on mean adult and pupae mortality, foraging activity,**	vegetable rate. Fenoxycarb was used as the control reference, which is expected to exert toxic effects on larvae, not adults. Control and reference bees were sprayed while foraging, while the treatment hives were sprayed when bees were not present. There was rainfall during the course of the exposure phase, which may have resulted in reduced exposure to the test material in both the treatment hives and the reference control hives. In the report, residues of cyclaniliprole were detected in pollen of control bees at 0.097 mg/kg, whereas no residues were detected in pollen of treated bees. No explanation was found by the study author. Although not statistically significant, there was higher mortality in the treatment hives on the day of application (following treatment, DAT 0aa). Variability in the data may have resulted in lower statistical sensitivity. The low sensitivity of the reference toxicant may indicate an issue with the study (and lack of exposure).	

Study design	Conclusion	Uncertainties	PMRA #
and flowers were collected.	**colony strength, conditions of the colony performance and brood development were observed. Although not statistically significant, there was a trend of higher mortality in the treatment group on the day after application that was transient and returned to control levels after 1 day. Mean adult mortality on the day following application (DAT 0) was 60.3, 108 and 46.7 dead bees/colony in the control, treatment and reference control hives, respectively. The mean adult mortality was similar among all hives by day 1 (range of 2.3 to 5.7 dead bees), and similar overall (DAT 0 to 28 aa). Foraging activity declined by day 7 in all hives (range of 2.8 to 4.5 bees/m^2). The brood termination rate in the test item treatment group was not statistically different when compared to the untreated control or the reference toxicant. The low sensitivity of the reference toxicant may indicate an issue with the study (and lack of exposure). It must be considered that due to unsuitable and rainy weather conditions during the exposure phase after application (DAT 1 to DAT 6) the exposure of honey bees to dried residues (the test item and reference item) was significantly decreased (i.e., low foraging activity and wash-off of the treatments due to rain). Therefore, the set validity criteria for the reference item were not met.** <u>Residues and exposure:</u> The residues of Cyclaniliprole 50SL found in pollen and flowers indicate exposure of the honey bees to the residues of the test item. Residues were not detected in nectar. In pollen combs and pollen traps from treated hives, residues were 1.114 and 0.810 mg/kg, respectively. In flowers from the treated tunnels, residues ranged from 0.607 to 2.127 mg/kg. It is noted that pollen from control hive bees had residues of cyclaniliprole at 0.097		

Study design	Conclusion	Uncertainties	PMRA #
	mg/kg, and residues from treated hive bees were below LOQ (0.005 mg/kg).		
Tier III (field studies)			
Study type: Field study Application rate: 2 × 40 g a.i./ha, 14 day interval) Replicates: 4 hives (3 for biological assessment and 1 residue monitoring) Colony size before exposure: 18303.8 bees in the control and 15637.5 bees in the test item. Product applied: Cyclaniliprole 50SL (End-Use Product) Crop: *Phacelia tanacetifolia* Application timing: The first application was made before full flowering and before bee hives were present. The second application was made during full flower, in the evening after bee foraging activity. Exposure period: Colonies were in fields for 28 days (7-day acclimation period and 21 days of treatment). Following the second application (DAT 7), bees were moved to a grassland site. Year: 2014 Location: Germany Field size: 5040 m^2 Observation/ endpoints: Hives were observed for	Adult mortality: Although not significantly different, mean mortality of adult forager bees was 3 times higher (41.3 bees/colony) in the treatment hives compared to the control (12.6 bees/colony) 11 days after the first application was made (before plants were in bloom). Bees were not present in the fields for the first application. However, cyclaniliprole is not systemic and the application was pre-bloom, therefore, negligible amounts of active ingredient are anticipated in pollen and/or nectar from the first application. Following the second application, on day 1, mean mortality was 26.5 dead bees in the treatment hives compared to 5.8 in the control. Mean mortality (day 0-7 after second application) was significantly higher at the test item hives (36.4 bees/colony) compared to the controls (14.9 bees/colony). Daily mean mortality during the post application phase (DAST 8 to 28) was not significantly different, however, it was 3 times higher at the treatment hives compared to control hives (178.5 and 44.6 bees/colony, respectively). It is noted that there is high variation in the mortality data. Mortality was consistently higher in the treatment hives over the course of the study. Brood and colony condition: Pupal mortality after the first and second applications, and also during post-exposure phase were similar between the treatment and control hives, although it is noted that there was almost twice as many dead pupae in the treatment hives during the post-exposure phase (15 compared to 8 dead pupae in the control).	The single rate of application (40 g a.i./ha) was lower than the proposed single maximum application rate in Canada (80 g a.i./ha) and maximum annual rate in Canada (300 g a.i./ha). On the evening and the following day of the 1st daytime application, rain occurred. The next rain event occurred on day 8 following the 2nd test item night application (after removing and relocating the colonies to the grassland area). However, residues were detected in pollen traps and combs, and in flowers. Therefore, it appears that exposure did occur. The high variability in mortality data may have resulted in the inability to determine effects. It is noted that adult mortality was typically 3 times higher in the treatment hives compared to the control hives. Mortality was up to 2783, 3759 and 4257 dead adult bees on day 10, 16, 22 and 28, respectively, in the treatment hives. Other chemicals were not analysed, and thus, it is unknown if hives were exposed to other chemicals. There were limited replicates. The study author indicated that robbing led to higher mortality due to study design, however, this would be expected in control hives as well. No overwintering observations were made.	2399054

Study design	Conclusion	Uncertainties	PMRA #
mortality of adult bees and pupa, brood development (termination rate), foraging activity, and behavioural abnormalities. <u>Residue collection:</u> Residues in nectar combs and bulbs, and pollen combs, pollen from traps, pollen from bees and flowers were collected.	<u>Foraging:</u> Foraging was similar between the treatment and control hives following the first application and also the post-exposure period from DAST 1 to 7 only. However, foraging was significantly lower in the treatment hives following the second application (on DAST 0 only). The significant decrease of foraging activity on day 0 and increased adult mortality on day 1 after the 2nd treatment application and during the exposure phase (day 0 to 7) was only temporary. **<u>Summary:</u>** **Overall, no adverse effects on pupae mortality, colony strength, conditions of the colony performance and brood development were observed. Mean adult mortality after the second application between DAST 0 and7 (36.4 dead bees/colony) was significantly higher than the control (14.9 dead bees/colony). There was no significant difference in mortality between the treatment and control hives during the remainder of the study. However, following the 2nd application, mean mortality was numerically higher in the treated hives (26.5 dead bees/colony) compared to the control hives (5.8 dead bees/colony) for 1 day and overall, the daily mean mortality post-application was numerically higher in the treated hives (178.5 dead bees/colony) compared to the control hives (44.6 dead bees/colony). The brood termination rate in the test item treatment group was lower when compared to the untreated control.** **The significant decrease of foraging activity after the second application and the observed statistically significantly increased adult mortality for 1 day after the 2nd treatment application during the**		

Study design	Conclusion	Uncertainties	PMRA #
	exposure phase (day 0 to 7) was only transient. Residues and exposure: The residues of Cyclaniliprole 50SL found in pollen and flowers indicate exposure of the honey bees to the residues of the test item. From the treated hives, pollen from traps and combs were 0.027 and 0.731 mg/kg, respectively, and residues in flowers ranged from 0.241 to 1.586 mg/kg. No residues were detected in nectar. No residues were detected in the control plants or hives.		
Study type: Field study Application rate: 2 × 40 g a.i./ha, 14 day interval) Replicates: 4 hives (3 for biological assessment and 1 residue monitoring) Colony size before exposure: 12334 bees in the control and 12415 bees in the test item. Product applied: Cyclaniliprole 50SL (End-Use Product) Crop: *Phacelia tanacetifolia* Application timing: The first application was made before full flowering and before bee hives were present. The second application was made during full flower, in the evening after bee foraging activity. Plot size: Test item treated plot of about 5590 m^2 and an untreated control plot of about 5248 m^2.	Adult mortality: Mortality levels during the pre-application period (DAST -3 to DAST -1 before the evening application, and after the first application before bloom and hive introductions) in the test item treatment group were generally higher and significantly different when compared to the control group. The first treatments were made 11 days before bees were introduced into the fields and the crop was not in bloom. However, there was no statistically significant difference on the overall daily mean mortality between the test item (25.4 bees/colony) and the control group (5.9 bees/colony). It is noted that cyclaniliprole is not systemic and the first application was pre-bloom, therefore, negligible amounts of active ingredient are anticipated in pollen and/or nectar from the first application. On DAST 0 and DAST 1 after the 2nd test item evening application of Cyclaniliprole 50SL, mortality in the test item treatment (9.8 and 2.8 dead bees per colony, respectively) was not significantly increased when compared to the control treatment (5.0 and 1.8 bees per colony, respectively). There was increased mortality on DAST 5 and 6 (19.5 and 2.3 bees/colony, respectively) in the test item treatment group which was below the daily mean mortality level during the pre-exposure	The single rate of application was lower than the proposed single maximum application rate in Canada (80 g a.i./ha) and maximum annual rate in Canada (300 g a.i./ha). Other chemicals were not analysed, and thus, it is unknown if hives were exposed to other chemicals. There were limited replicates. The timing of foraging activity differed in some instances between the control and treatment hives, and as such, the lower foraging activity in the treatment hives after application may have been from temperature (as proposed by the study author). The control and treatment plots were 3.06 km apart. No residues were detected in the control hives. The exposure period was only 8 days. No overwintering observations were made.	2399059

Study design	Conclusion	Uncertainties	PMRA #
Location: Albacete, Spain Year: 2013 Exposure period: The colony progress (development) was observed until day 27 following the 2nd daytime application. The exposure period of the bees in the treated and untreated plots was 8 days. In the evening on day 8, the colonies were removed from both treatment plots and relocated to a grassland area. Observation/ endpoints: Hives were observed for mortality of adult bees and pupa, brood development (termination rate), foraging activity, and behavioural abnormalities. Residue collection: Residues in nectar combs and bulbs, and pollen combs, pollen from traps, pollen from bees and flowers were collected.	phase (DAST -3 to DAST -1). Overall daily mean mortality (DAST 0 to 8) in the test item group (7.0 bees/colony) was not significantly increased when compared to the control group (4.7 bees/colony) (Student t-test, one-sided greater, $\alpha = 0.05$). During the post-exposure phase (DAST 9 to 27), the daily mean values between the test item treatment field and the untreated control field were comparable and not statistically significantly different. Overall daily mean mortality in the test item group during the post exposure phase (DAST 9 to 27) and post application phase (DAST 0 to 27) was 12.6 and 10.8 bees/colony, respectively. Hence, the test/treatment results are not statistically significantly different when compared to the control (6.5 and 5.9 bees per colony, respectively). Brood development: Over the course of the study, during DAST -3 to -1 after second application (DAST 0 to 8), and during post-exposure (DAST 9 to27), there were less than 0.3 dead pupae in the treatment and control hives. It is noted that the brood termination rate in the test item treatment group was lower (7.9%) when compared to the untreated control (15%), but not statistically significant. There was no indication of any adverse effects of the test item on the condition of the bee colonies or colony strength. Foraging: Mean foraging was not significantly different between control and treatment hives during DAST -3 to -1 and during the post-exposure phase		

Study design	Conclusion	Uncertainties	PMRA #
	(DAST 0 to 8). However, on day 0 after application, foraging was significantly lower in the treatment group (3.5 bees/m^2/colony) compared to the control (5.8 bees/m^2/colony). The study author proposed that cooler temperature during the time of observation in the treatment hives was likely the result of the lower foraging activity. On DAST 0, a high aggressiveness of the honeybees was observed in the test item treated plot following the 2nd daytime application of Cyclaniliprole 50SL. **Summary:** **Overall, no adverse effects on adult and pupae mortality, colony strength, conditions of the colony performance and brood development were observed. There were no significant treatment-related differences between the treatment and control hives. There was lower foraging activity in the treatment hives on the day of application that was attributed to the differences in weather when the treated foraging observations were collected on a different day than the control.** Residues and exposure: The residues of Cyclaniliprole 50SL found in pollen and flowers indicate exposure of the honey bees to the residues of the test item. No residues were detected in nectar. At the treatment site, residues in pollen traps ranged from 0.047 to 0.497 mg/kg and residues in flowers ranged from 0.124 to 3.331 mg/kg. No residues were detected in the control plants or hives.		

Study design	Conclusion	Uncertainties	PMRA #
<u>Study type:</u> Field study <u>Application rate:</u> 40 g a.i./ha <u>Replicates</u>: 4 hives (3 for biological assessment and 1 residue monitoring) <u>Colony size before exposure</u>: 13828.8 bees in the control and 12853.8 bees in the test item. <u>Product applied:</u> Cyclaniliprole 50SL (End-Use Product) <u>Crop:</u> *Phacelia tanacetifolia* <u>Year:</u> 2013 <u>Location:</u> Valencia, Spain <u>Application timing:</u> Application was made during full flower during the day when bees were active. <u>Field size</u>: Test item treated plot of about 4791 m^2 and an untreated control plot of about 5335 m^2. <u>Exposure period:</u> The colony progress (development) was observed until DAT 27 following the daytime application. The exposure period of the bees in the treated and untreated plots was 9 days. On DAT 9, the colonies were removed from both treatment plots and relocated to a grassland area	<u>Adult mortality:</u> Mortality levels during the pre-application period (DAT -3 to DAT 0 before application) in the test item treatment group were generally higher but not significantly different when compared to the control group.The overall daily mean mortality between the test item (10.7 bees/colony) and the control group (5.6 bees/colony) was low. On DAT 0 after the test item application of Cyclaniliprole 50SL, mortality in the test item treatment (326.3 dead bees per colony) was significantly increased when compared to the control treatment (3.8 bees per colony). Furthermore, mortality in the test item treatment group was significantly increased on DAT 1, 3, 6 and 7 with 46.8, 10.3, 11.0 and 3.8 bees/colony, when compared to the control treatment with 0.0, 3.3, 2.5 and 0.3 bees / colony, respectively. The increased mortality on DAT 3, 6 and 7 in the test item treatment group was below or similar to the daily mean mortality level from DAT -3 to DAT 0ba. Overall daily mean mortality (DAT 0aa to 9) in the test item group (43.4 bees/colony) was significantly increased when compared to the control group (6.2 bees/colony). During the post-exposure phase (DAT 10 to 28), the daily mean values between the test item treatment field and the untreated control field were comparable and not significantly different when compared to the control group with one exception on DAT 12 (47.3 bees/colony) in the test item treatment group. Overall daily mean mortality in the test item group during the post-exposure phase (DAT 10 to 28) and post- application phase (DAT 0a.a. to 28) was 23.6 and 30.4 bees/colony, respectively.	The single rate of application (40 g a.i./ha) was lower than the proposed maximum single application rate in Canada (80 g a.i./ha) or maximum annual rate in Canada (300 g a.i./ha). Other chemicals were not analysed, and thus, it is unknown if hives were exposed to other chemicals. The exposure period was 10 days. No overwintering observations.	2399062

Study design	Conclusion	Uncertainties	PMRA #
Observation/ endpoints: Hives were observed for mortality of adult bees and pupa, brood development (termination rate), foraging activity, and behavioural abnormalities. Residue collection: Residues in nectar combs and bulbs, and pollen combs, pollen from traps, pollen from bees and flowers were collected.	Brood development: Over the course of the study, during DAST -3 to -1, after second application (DAST 0 to 8), and during post-exposure (DAST 9 to 27), there were less than 0.5 dead pupae in the treatment and control hives. There was no indication of any adverse effects of the test item on the condition of the bee colonies or colony strength. Brood termination was 2.6 and 3.3% in the control and treatment hives, respectively. Foraging: Foraging was significantly higher in the treatment hives on day 0 shortly before application (34.3 bees/m^2/colony/day) compared to controls (8.5 bees/m^2/colony/day), DAT -3 to 0 (29.4 bees/m^2/colony/day) compared to controls (9.4 bees/m^2/colony/day) and also on day 0 (29.0 bees/m^2/colony/day) compared to controls (6.6 bees/m^2/colony/day). **Summary:** **Overall, regarding the colony performance, no adverse effects on pupae mortality, foraging activity, colony strength, or brood development were observed. The observed increased mortality of worker bees was increased significantly after application (treatment: 326.3 dead bees/colony; control: 3.8 dead bees/colony) and remained significantly different, although numerically lower for up to 7 days. On days, 3, 6 and 7 (treated: 10.3, 11 and 3.8 dead bees/colony compared to control: 3.3, 2.5 and 0.3 dead bees/colony), however, these were relatively low and comparable to the mortality prior to exposure in the treatment hives. The brood termination rate in the test item treatment group was very low and similar when compared to the control group.**		

Study design	Conclusion	Uncertainties	PMRA #
	Residues and exposure: The residues of Cyclaniliprole 50SL found in pollen and flowers indicate exposure of the honey bees to the residues of the test item. No residues were detected in nectar. At the treatment site, residues in pollen combs were 0.101 mg/kg, residues in pollen traps ranged from 0.047 to 0.102 mg/kg, residues in pollen from bees ranged from 0.170 to 1.547 mg/kg and residues on flowers ranged from 0.257 to 1.324 mg/kg. No residues were detected in the control plot hives or plants.		
Study type: Field study Application rate: 60 g a.i./ha × 2, made 5-6 days apart) Replicates: 4 hives (3 for biological assessment and 1 residue monitoring) Colony size before exposure: 3200 bees in the control and 4100 bees in the test item. Product applied: Cyclaniliprole 50SL (End-Use Product) Crop: Canola. Application timing: The first application was made during early mid-bloom in the evening after bee foraging activity. The second application was made 5-6 days later in the evening after bee foraging activity. Field size: The trial was carried out on field plots of about 10 acres Year: 2015	Adult mortality: Mean mortality during the pre-application period (DAST -3 to DAST -1 before the first evening application) was 13.79 bees/colony in the treatment hives and 11.62 bees/colony in the control hives, indicating that the colonies among the treatment groups were comparable. Overall daily mean mortality during the exposure phase (1-12 DAFA) in the test item group (34 bees/colony) was significantly increased when compared to the control group (19 bees/colony). There appeared to be a trend of higher mortality following application. On the first day following the first application, mean mortality was approximately 88 dead bees in the treatment hives. In comparison, the control had approximately 11 dead bees. There was also elevated mortality following the second application. Between 2 and 5 days after the second application, mortality in the treatment hives reached approximately 131 dead bees compared to 9 dead bees in the control. Overall during the post-exposure phase (13 to 48 DAFA), the daily mean values between the test item group (77 bees/colony) and the untreated control group (66 bees/colony) were comparable and not	The study report provided inadequate information on the study sites. Missing information included the size of the plots and description of crops grown in adjacent areas. The study however, did mention that "no other attractive arable crops were observed in the surroundings of the test item and control plot which were 4.8 km apart". There were limited replicates. Colony condition assessments did not include quantifying the number of eggs, larvae, or honey storage cells. Low levels of cyclaniliprole (mean residues of 5-7 ppb) were detected in whole flowers and pollen of the untreated control sites. The study authors speculate that some spray drift may have occurred. The study report did not include raw data for observation of abnormal behaviour. The report noted observations of clumping in one of the treated plots, but did not state when they occurred relative to the pesticide applications. Other chemicals were not analysed, and thus, it is unknown if hives were exposed to other chemicals.	2614337

Study design	Conclusion	Uncertainties	PMRA #
Location: North Dakota Exposure duration: The exposure period of the bees in the treated and untreated plots was 12 days. In the evening on day 12, the colonies were removed from both treatment plots and relocated to a grassland area (until DAT 48). Observation/ endpoints: Hives were observed for mortality of adult bees and pupa, pollen stores, colony strength, brood development (termination rate), foraging activity, and behavioural abnormalities. Residues collected: Residues in nectar combs and bulbs, and pollen combs, pollen from traps, pollen from bees and flowers were collected.	significantly different. Brood development: No dead pupae were noted during the study for either the test item or the control group. Colony strength (expressed as the number of adults) was significantly lower in the treatment hives on day 48 after the second application. Relative to pre-exposure, colony strength was reduced by 8% in the treatment hives, whereas the strength was increased by 65% in the control. Food storage: The number of cells containing pollen decreased in both groups during the exposure period (CCA 1 to 3). Foraging activity: During the pre-application period (DAST -3 to -1 before application) daily mean foraging activity was 6.42 and 5.92 bees/m^2 in the test item and control group, respectively. From DAFA 1 to 12, foraging activity was comparable in both groups. The overall daily mean foraging activity was 5.73 bees /m^2 in the control group and 4.71 bees/m^2 in the test item treatment group. **Summary:** **Overall, there was a significant increase in adult bee mortality during the exposure phase of the study with a strong correlation between periods of elevated mortality and the timing of the applications. Cyclaniliprole 50SL did not significantly affect the brood nest or pollen stores, but did adversely affect colony strength in the post-exposure period. Colony strength was increased by 65% in the control and reduced by 8% in the treatment hives (as compared to pre-exposure strength).**	There were no overwintering observations. However, this study had observations up to 48 days after initiation of the study, which was longer than the other studies.	

Study design	Conclusion	Uncertainties	PMRA #
	<u>Residues and exposure:</u> The residues of Cyclaniliprole 50SL found in nectar, pollen, and flowers indicate exposure of the honey bees to the residues of the test item. Residues were also detected in control flower pollen. However, because no residues were detected in control pollen baskets and comb or bee bread, it is unknown if control bees were exposed to cyclaniliprole. Residues of cylaniliprole in floral nectar was 373.1 and 390.3 ppb at early- and mid-bloom and then declined to 3.7 ppb by late-bloom. Corresponding pollen residues were 344.8, 3049 and 25.7 ppb. Pollen baskets at early- and mid-bloom were 23.6 and 7.9 ppb, respectively, and corresponding bee bread residues were 5.1 and 3.8 ppb. By late-bloom the residues in pollen baskets and bee bread were below the level of detection (< 0.5 ppb). Comb nectar was found at 1.4 ppb during early-bloom sampling only.		

aa = after application
ba = before application
CCA = colony condition assessment
DAT = days after treatment
DAST = days after second treatment
DAFA = days after first application

Table 12 Screening Level Risk Assessment of Cyclaniliprole and End-use Product Cyclaniliprole 50SL Insecticide for Non-target Terrestrial Species Other than Birds and Mammals

Organism	Exposure	Endpoint Value	EEC	RQ	Level of Concern[1]
Invertebrates					
Earthworm, *Eisenia foetida*	Acute, technical cyclaniliprole	$LC_{50}/2$: > 500 mg a.i./kg soil	0.13 mg a.i./kg dry soil	< 0.1	Not exceeded
	Acute, Cyclaniliprole 50SL Insecticide	$LC_{50}/2$: > 23.15 mg a.i./kg soil	0.13 mg a.i./kg dry soil	< 0.1	Not exceeded
	Reproduction, technical cyclaniliprole	NOEC: 1000 mg a.i./kg soil	0.13 mg a.i./kg dry soil	< 0.1	Not exceeded
Terrestrial invertebrate, *Hypoaspis aculeifer*	Chronic, artificial soil, technical cyclaniliprole	NOEC: 555.56 mg a.i./kg soil	0.13 mg a.i./kg soil	< 0.1	Not exceeded
Terrestrial	Chronic, artificial	NOEC: 2.39 mg	0.13 mg a.i./kg soil	< 0.1	Not exceeded

<table>
<tr><th>Organism</th><th>Exposure</th><th>Endpoint Value</th><th>EEC</th><th>RQ</th><th>Level of Concern[1]</th></tr>
<tr><td>invertebrate, Folsomia candida</td><td>soil, technical cyclaniliprole</td><td>a.i./kg soil</td><td></td><td></td><td></td></tr>
<tr><td rowspan="7">Honey bee, Apis mellifera

Tier I assessment</td><td>Acute contact, adults, technical cyclaniliprole</td><td>LD_{50}: 0.952 µg a.i./bee</td><td>0.08 kg a.i./ha × 2.4 µg a.i./bee per kg/ha = 0.192 µg a.i./bee</td><td>0.2</td><td>Not exceeded</td></tr>
<tr><td>Acute contact, adults, Cyclaniliprole 50SL Insecticide</td><td>LD_{50}: 0.507 µg a.i./bee</td><td>0.08 kg a.i./ha × 2.4 µg a.i./bee per kg/ha = 0.192 µg a.i./bee</td><td>0.4</td><td>Not exceeded</td></tr>
<tr><td>Acute oral, adults, technical cyclaniliprole</td><td>LD_{50}: 0.702 µg a.i./bee</td><td>0.08 kg a.i./ha × 29 µg a.i./bee per kg/ha = 2.32 µg a.i./bee</td><td>3.3</td><td>Exceeded</td></tr>
<tr><td>Acute oral, adults, Cyclaniliprole 50SL Insecticide</td><td>LD_{50}: 0.2 µg a.i./bee</td><td>0.08 kg a.i./ha × 29 µg a.i./bee per kg/ha = 2.32 µg a.i./bee</td><td>12</td><td>Exceeded</td></tr>
<tr><td>Chronic oral, adults, Cyclaniliprole 50SL Insecticide</td><td>NOED: 0.023 µg a.i./bee/day</td><td>0.08 kg a.i./ha × 29 µg a.i./bee per kg/ha = 2.32 µg a.i./bee</td><td>101</td><td>Exceeded</td></tr>
<tr><td>Acute oral, larvae, technical cyclaniliprole</td><td>LD_{50}: 0.16 µg a.i./larva/day</td><td>0.08 kg a.i./ha × 12 µg a.i./larva per kg/ha = 0.96 µg a.i./larva</td><td>6.0</td><td>Exceeded</td></tr>
<tr><td>Chronic oral, larvae, technical cyclaniliprole</td><td>NOED: 0.0649 µg a.i./larva/day</td><td>0.08 kg a.i./ha × 12 µg a.i./larva per kg/ha = 0.96 µg a.i./larva</td><td>15</td><td>Exceeded</td></tr>
<tr><td rowspan="3">Honey bee, Apis mellifera

Tier I refined assessment</td><td>Acute oral, adults, Cyclaniliprole 50SL Insecticide</td><td>LD_{50}: 0.2 µg a.i./bee</td><td rowspan="3"><u>Residue[2]</u>

Early-bloom
Pollen: 344 ppb
Nectar: 373 ppb

Mid-bloom
Pollen: 3049 ppb
Nectar: 390 ppb

Late-bloom
Pollen: 25.7 ppb
Nectar: 3.7 ppb

<u>Estimated daily dose[3]</u>

Earlybloom
Pollen and nectar: 0.109 µg a.i./bee per day

Mid-bloom
Pollen and nectar: 0.114 µg a.i./bee per day

Late-bloom
Pollen and nectar: 0.001 µg a.i./bee per day</td><td>Early-bloom
0.5

Mid-bloom
0.6

Late-bloom
< 0.1</td><td>Early- bloom
Exceeded

Mid-bloom
Exceeded

Late- bloom
Not exceeded</td></tr>
<tr><td>Chronic oral, adults, Cyclaniliprole 50SL Insecticide</td><td>NOED: 0.023 µg a.i./bee per day</td><td>Early-bloom
4.7

Mid-bloom
5.0

Late-bloom
< 0.1</td><td>Early- bloom
Exceeded

Mid-bloom
Exceeded

Late- bloom
Not exceeded</td></tr>
<tr><td>Acute oral, larvae, technical cyclaniliprole</td><td>LD_{50}: 0.16 µg a.i./larva</td><td>Early-bloom
0.3

Mid-bloom</td><td>Not exceeded</td></tr>
</table>

Organism	Exposure	Endpoint Value	EEC	RQ	Level of Concern[1]
				0.3 *Late-bloom* < 0.1	
	Chronic oral, larvae, technical cyclaniliprole	NOED: 0.0649 µg a.i./larva		*Early-bloom* 0.7 *Mid-bloom* 0.9 *Late-bloom* < 0.1	Not exceeded
Predatory arthropod, *Typhlodromus pyri*	Glass plates, Cyclaniliprole 50SL Insecticide	LR_{50}: 105 g a.i./ha	In-field: 174 g a.i./ha	1.7	Not exceeded
			Off-field (174 g a.i./ha × 74% drift[4]): 129 g a.i./ha	1.2	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[5]): 19 g a.i./ha	0.2	Not exceeded
Parasitoid arthropod, *Aphidius rhopalosiphi*	Glass plates, Cyclaniliprole 50SL Insecticide	LR_{50}: 0.507 g a.i./ha	In-field: 174 g a.i./ha	**343**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[4]): 129 g a.i./ha	**254**	Exceeded
			Off-field (174 g a.i./ha × 11% drift[5]): 19 g a.i./ha	**38**	Exceeded
Vascular plants	Seedling emergence, Cyclaniliprole 50SL Insecticide	ER_{25}: > 1000 g a.i./ha	298 g a.i./ha	0.3	Not exceeded
	Vegetative vigour, Cyclaniliprole 50SL Insecticide	ER_{25}: > 1000 g a.i./ha	174 g a.i./ha	0.2	Not exceeded

[1] Level of concern = 1 for most species; 0.4 for acute risk to pollinators; and 2 for glass plate studies using the standard beneficial arthropod test species, *Typhlodromus pyri* and *Aphidius rhopalosiphi*

[2] Highest residue values were derived from PMRA# 2614337.

[3] Daily consumption rate used for foraging adult worker bees: 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. Example calculation for estimated daily dose for adult forager bees, mid-bloom: Pollen: 3049 ppb × 0.041 mg/day/1.0 × 10^6) = 1.25 × 10^{-4} µg a.i./bee per day; Nectar: 390 ppb × 292 mg/day/1.0 × 10^6 = 0.114 µg a.i./bee per day; Pollen and nectar: 1.25 × 10^{-4} µg a.i./bee per day + 0.114 µg a.i./bee per day = 0.114 µg a.i./bee per day.

[4] 74% drift from early season airblast application

[5] 11% drift from field sprayer application using minimum spray droplet size of ‘fine’. Even though fieldspray application equipment would not be used on stone fruits which is the use pattern followed to derive expected environmental concentrations for this risk assessment, this method of application with lower drift serves to bracket the risk from drift using all application methods.

Table 13 Screening Level Risk Assessment of Cyclaniliprole for Birds and Mammals using Maximum Residues Expected Following Multiple Applications on Stone fruits (1 × 60 g a.i./ha + 3 × 80 g a.i./ha at 7-day intervals). Values in Bold Indicate Exceedances of the Level of Concern.

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	EDE (mg a.i./kg bw)[1]	RQ
Small Bird (0.02 kg)				
Acute	> 200	Insectivore	14.13	< 0.1
Reproduction	8.80	Insectivore	14.13	**1.6**
Medium-Sized Bird (0.1 kg)				
Acute	> 200	Insectivore	11.03	< 0.1
Reproduction	8.80	Insectivore	11.03	**1.3**
Large-Sized Bird (1 kg)				
Acute	> 200	Herbivore (short grass)	7.12	< 0.1
Reproduction	8.80	Herbivore (short grass)	7.12	0.8
Small Mammal (0.015 kg)				
Acute	> 200	Insectivore	8.13	< 0.1
Reproduction	1046	Insectivore	8.13	< 0.1
Medium-Sized Mammal (0.035 kg)				
Acute	> 200	Herbivore (short grass)	15.76	< 0.1
Reproduction	1046	Herbivore (short grass)	15.76	< 0.1
Large-Sized Mammal (1 kg)				
Acute	> 200	Herbivore (short grass)	8.42	< 0.1
Reproduction	1046	Herbivore (short grass)	8.42	< 0.1

[1] 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) = $0.398(\text{BW in g})^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{BW in g})^{0.651}$.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = $0.235(\text{BW in g})^{0.822}$
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.

Table 14 Further Characterization of the Risk of the End-use Product Cyclaniliprole 50SL Insecticide to Non-target Predatory and Parasitic Arthropods Using Results from Extended Laboratory and Aged Residue Studies

Organism	Exposure	Endpoint Value	EEC	RQ	Level of Concern[1]
Parasitoid arthropod, *Aphidius rhopalosiphi*	Extended laboratory/aged residues, leaves, Cyclaniliprole 50SL Insecticide	0 DAT LR_{50}: 4.32 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**32**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation	**3.0**	Exceeded

Organism	Exposure	Endpoint Value	EEC	RQ	Level of Concern[1]
			distribution factor): 13 g a.i./ha		
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	0.4	Not exceeded
		0 DAT ER_{50}: 4.09 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**34**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 12.9 g a.i./ha	**3.1**	Exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	0.5	Not exceeded
		14 DAT LR_{50}: 24.1 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**5.8**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 13 g a.i./ha	0.5	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	< 0.1	Not exceeded
		14 DAT ER_{50}: 12.68 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**11**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 13 g a.i./ha	**1.0**	Exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	0.2	Not exceeded
		28 and 56 DAT LR_{50}: > 80 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**< 1.7**	Possibly exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 13 g a.i./ha	< 0.2	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	< 0.1	Not exceeded
		28 DAT ER_{50}: 47.74 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**2.9**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 13 g a.i./ha	0.3	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	< 0.1	Not exceeded
		56 DAT ER_{50}: > 80 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**< 1.7**	Possibly exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 13 g a.i./ha	< 0.2	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation	< 0.1	Not exceeded

Organism	Exposure	Endpoint Value	EEC	RQ	Level of Concern[1]
			distribution factor): 1.9 g a.i./ha		
Foliar-dwelling arthropod, *Coccinella septempunctata*	Extended laboratory/aged residues, leaves, Cyclaniliprole 50SL Insecticide	0 DAT LR_{50}: 28.1 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**5.0**	Exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 12.9 g a.i./ha	0.5	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	< 0.1	Not exceeded
		0 DAT ER_{50}: > 27.2 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**< 5.1**	Possibly exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 12.9 g a.i./ha	< 0.5	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	< 0.1	Not exceeded
		28 and 56 DAT LR_{50} and ER_{50}: > 80 g a.i./ha	In-field (174 g a.i./ha × 0.8 foliar deposition factor): 139 g a.i./ha	**< 1.7**	Possibly exceeded
			Off-field (174 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 13 g a.i./ha	< 0.2	Not exceeded
			Off-field (174 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 1.9 g a.i./ha	< 0.1	Not exceeded
Soil-dwelling arthropod, *Aleochara bilineata*	Extended laboratory/aged residues, soil, Cyclaniliprole 50SL Insecticide	0 DAT LR_{50}: 84.3 g a.i./ha	In-field (298 g a.i./ha × 0.8 soil deposition factor): 238 g a.i./ha	**2.8**	Exceeded
			Off-field (298 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 22 g a.i./ha	0.3	Not exceeded
			Off-field (298 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 3.3 g a.i./ha	< 0.1	Not exceeded
		0 DAT ER_{50}: > 80 g a.i./ha	In-field (298 g a.i./ha × 0.8 soil deposition factor): 238 g a.i./ha	**< 3.0**	Possibly exceeded
			Off-field (298 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 22 g a.i./ha	< 0.3	Not exceeded
			Off-field (298 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 3.3 g a.i./ha	< 0.1	Not exceeded
		14, 28 and 56 DAT LR_{50} and ER_{50}: > 80 g a.i./ha	In-field (298 g a.i./ha × 0.8 soil deposition factor): 238 g a.i./ha	**< 3.0**	Possibly exceeded

Organism	Exposure	Endpoint Value	EEC	RQ	Level of Concern[1]
			Off-field (298 g a.i./ha × 74% drift[2] × 0.1 vegetation distribution factor): 22 g a.i./ha	< 0.3	Not exceeded
			Off-field (298 g a.i./ha × 11% drift[3] × 0.1 vegetation distribution factor): 3.3 g a.i./ha	< 0.1	Not exceeded

[1] Level of concern = 1
[2] 74% drift from early season airblast application
[3] 11% drift from field sprayer application using minimum spray droplet size of 'fine'. Even though fieldspray application equipment would not be used on stone fruits which is the use pattern followed to derive expected environmental concentrations for this risk assessment, this method of application with lower drift serves to bracket the risk from drift using all application methods.

Table 15 Risk Assessment of Cyclaniliprole for Birds Using Maximum Residues Expected Following Multiple Applications on Stone Fruits (1 × 60 g a.i./ha + 3 × 80 g a.i./ha at 7-day Intervals). Values in Bold Indicate Exceedances of the Level of Concern.

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	On-field		Off Field[2]	
			EDE (mg a.i./kg bw)[1]	RQ	EDE (mg a.i./kg bw)[1]	RQ
Small Bird (0.02 kg)						
Acute	> 200	Insectivore	14.13	< 0.1	10.45	< 0.1
	> 200	Granivore (grains and seeds)	2.19	< 0.1	1.62	< 0.1
	> 200	Frugivore (fruit)	4.37	< 0.1	3.24	< 0.1
Dietary	> 100	Insectivore	14.13	< 0.1	10.45	< 0.1
	> 100	Granivore (grains and seeds)	2.19	< 0.1	1.62	< 0.1
	> 100	Frugivore (fruit)	4.37	< 0.1	3.24	< 0.1
Reproduction	8.8	Insectivore	14.13	**1.6**	10.45	**1.2**
	8.8	Granivore (grains and seeds)	2.19	0.3	1.62	0.2
	8.8	Frugivore (fruit)	4.37	0.5	3.24	0.4
Medium-Sized Bird (0.1 kg)						
Acute	> 200	Insectivore	11.03	< 0.1	8.16	< 0.1
	> 200	Granivore (grains and seeds)	1.71	< 0.1	1.26	< 0.1
	> 200	Frugivore (fruit)	3.41	< 0.1	2.53	< 0.1
Dietary	> 100	Insectivore	11.03	< 0.2	8.16	< 0.1
	> 100	Granivore (grains and seeds)	1.71	< 0.1	1.26	< 0.1
	> 100	Frugivore (fruit)	3.41	< 0.1	2.53	< 0.1
Reproduction	8.8	Insectivore	11.03	**1.3**	8.16	0.9
	8.8	Granivore (grains and seeds)	1.71	0.2	1.26	0.1
	8.8	Frugivore (fruit)	3.41	0.4	2.53	0.3
Large-Sized Bird (1 kg)						
Acute	> 200	Insectivore	3.22	< 0.1	2.38	< 0.1
	> 200	Granivore (grains and seeds)	0.5	< 0.1	0.37	< 0.1
	> 200	Frugivore (fruit)	1	< 0.1	0.74	< 0.1
	> 200	Herbivore (short grass)	7.12	< 0.1	5.27	< 0.1
	> 200	Herbivore (long grass)	4.35	< 0.1	3.22	< 0.1
	> 200	Herbivore (broadleaf plants)	6.59	< 0.1	4.88	< 0.1

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	On-field		Off Field[2]	
			EDE (mg a.i./kg bw)[1]	RQ	EDE (mg a.i./kg bw)[1]	RQ
Dietary	> 100	Insectivore	3.22	< 0.1	2.38	< 0.1
	> 100	Granivore (grains and seeds)	0.5	< 0.1	0.37	< 0.1
	> 100	Frugivore (fruit)	1	< 0.1	0.74	< 0.1
	> 100	Herbivore (short grass)	7.12	< 0.1	5.27	< 0.1
	> 100	Herbivore (long grass)	4.35	< 0.1	3.22	< 0.1
	> 100	Herbivore (broadleaf plants)	6.59	< 0.1	4.88	< 0.1
Reproduction	8.8	Insectivore	3.22	0.4	2.38	0.3
	8.8	Granivore (grains and seeds)	0.5	0.1	0.37	< 0.1
	8.8	Frugivore (fruit)	1	0.1	0.74	0.1
	8.8	Herbivore (short grass)	7.12	0.8	5.27	0.6
	8.8	Herbivore (long grass)	4.35	0.5	3.22	0.4
	8.8	Herbivore (broadleaf plants)	6.59	0.8	4.88	0.6

[1] 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) = $0.398(\text{BW in g})^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{BW in g})^{0.651}$.
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.
[2] Off-field drift calculated assuming 74% drift resulting from an early season airblast application.

Table 16 Risk Assessment of Cyclaniliprole for Birds using Mean Residues Expected Following Multiple Applications on Stone Fruits (1 × 60 g a.i./ha + 3 × 80 g a.i./ha at 7-day Intervals). Values in Bold Indicate Exceedances of the Level of Concern.

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	On-field		Off Field[2]	
			EDE (mg a.i./kg bw)[1]	RQ	EDE (mg a.i./kg bw)[1]	RQ
Small Bird (0.02 kg)						
Acute	> 200	Insectivore	9.76	< 0.1	7.22	< 0.1
	> 200	Granivore (grains and seeds)	1.04	< 0.1	0.77	< 0.1
	> 200	Frugivore (fruit)	2.09	< 0.1	1.54	< 0.1
Dietary	> 100	Insectivore	9.76	< 0.1	7.22	< 0.1
	> 100	Granivore (grains and seeds)	1.04	< 0.1	0.77	< 0.1
	> 100	Frugivore (fruit)	2.09	< 0.1	1.54	< 0.1
Reproduction	8.8	Insectivore	9.76	**1.1**	7.22	0.8
	8.8	Granivore (grains and seeds)	1.04	0.1	0.77	0.1
	8.8	Frugivore (fruit)	2.09	0.2	1.54	0.2
Medium-Sized Bird (0.1 kg)						
Acute	> 200	Insectivore	7.61	< 0.1	5.63	< 0.1
	> 200	Granivore (grains and seeds)	0.81	< 0.1	0.6	< 0.1
	> 200	Frugivore (fruit)	1.63	< 0.1	1.2	< 0.1

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	On-field		Off Field[2]	
			EDE (mg a.i./kg bw)[1]	RQ	EDE (mg a.i./kg bw)[1]	RQ
Dietary	> 100	Insectivore	7.61	< 0.1	5.63	< 0.1
	> 100	Granivore (grains and seeds)	0.81	< 0.1	0.6	< 0.1
	> 100	Frugivore (fruit)	1.63	< 0.1	1.2	< 0.1
Reproduction	8.8	Insectivore	7.61	0.9	5.63	0.6
	8.8	Granivore (grains and seeds)	0.81	0.1	0.6	0.1
	8.8	Frugivore (fruit)	1.63	0.2	1.2	0.1
Large-Sized Bird (1 kg)						
Acute	> 200	Insectivore	2.22	< 0.1	1.64	< 0.1
	> 200	Granivore (grains and seeds)	0.24	< 0.1	0.18	< 0.1
	> 200	Frugivore (fruit)	0.48	< 0.1	0.35	< 0.1
	> 200	Herbivore (short grass)	2.53	< 0.1	1.87	< 0.1
	> 200	Herbivore (long grass)	1.42	< 0.1	1.05	< 0.1
	> 200	Herbivore (broadleaf plants)	2.18	< 0.1	1.61	< 0.1
Dietary	> 100	Insectivore	2.22	< 0.1	1.64	< 0.1
	> 100	Granivore (grains and seeds)	0.24	< 0.1	0.18	< 0.1
	> 100	Frugivore (fruit)	0.48	< 0.1	0.35	< 0.1
	> 100	Herbivore (short grass)	2.53	< 0.1	1.87	< 0.1
	> 100	Herbivore (long grass)	1.42	< 0.1	1.05	< 0.1
	> 100	Herbivore (broadleaf plants)	2.18	< 0.1	1.61	< 0.1
Reproduction	8.8	Insectivore	2.22	0.3	1.64	0.2
	8.8	Granivore (grains and seeds)	0.24	< 0.1	0.18	< 0.1
	8.8	Frugivore (fruit)	0.48	< 0.1	0.35	< 0.1
	8.8	Herbivore (short grass)	2.53	0.3	1.87	0.2
	8.8	Herbivore (long grass)	1.42	0.2	1.05	0.1
	8.8	Herbivore (broadleaf plants)	2.18	0.3	1.61	0.2

[1] 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) = $0.398(\text{BW in g})^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{BW in g})^{0.651}$.
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.
[2] Off-field drift calculated assuming 74% drift resulting from an early season airblast application.

Table 17 Reproductive Risk Assessment of Cyclaniliprole for Birds Using the Lowest Observable Effects Level (LOEL) and Maximum Residues Expected Following Multiple Applications on Stone Fruits (1 × 60 g a.i./ha + 3 × 80 g a.i./ha at 7-day Intervals)

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	On-field		Off Field[2]	
			EDE (mg a.i./kg bw)[1]	RQ	EDE (mg a.i./kg bw)[1]	RQ
Small Bird (0.02 kg)						
Reproduction	25.7	Insectivore	14.13	0.6	10.45	0.4
	25.7	Granivore (grains and seeds)	2.19	0.1	1.62	0.1
	25.7	Frugivore (fruit)	4.37	0.2	3.24	0.1
Medium-Sized Bird (0.1 kg)						
Reproduction	25.7	Insectivore	11.03	0.4	8.16	0.3
	25.7	Granivore (grains and seeds)	1.71	0.1	1.26	0.1
	25.7	Frugivore (fruit)	3.41	0.1	2.53	0.1
Large-Sized Bird (1 kg)						
Reproduction	25.7	Insectivore	3.22	0.1	2.38	0.1
	25.7	Granivore (grains and seeds)	0.5	< 0.1	0.37	< 0.1
	25.7	Frugivore (fruit)	1	< 0.1	0.74	< 0.1
	25.7	Herbivore (short grass)	7.12	0.3	5.27	0.2
	25.7	Herbivore (long grass)	4.35	0.2	3.22	0.1
	25.7	Herbivore (broadleaf plants)	6.59	0.3	4.88	0.2

[1] 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) = $0.398(\text{BW in g})^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = $0.648(\text{BW in g})^{0.651}$.
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.
[2] Off-field drift calculated assuming 74% drift resulting from an early season airblast application.

Table 18 Toxicity of Cyclaniliprole, its Transformation Products and the End-use Product Cyclaniliprole 50SL Insecticide to Non-Target Aquatic Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
Freshwater species					
Daphnia magna	48-h Acute	Cyclaniliprole	EC_{50} = 0.0808 mg a.i./L	Very highly toxic	2398976
	48-h Acute	Cyclaniliprole 50SL (End-Use Product)	EC_{50} = 2.36 mg product/L (nominal) (0.0739 mg a.i./L, mean measured)	The end-use product is slightly more toxic than cyclaniliprole alone.	2502019
	48-h Acute	NK-1375	EC_{50} > 0.0543 mg/L (0% immobilization)	Not toxic up to the highest concentration tested, which approaches the limit of solubility in water (0.07	2398979

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
				mg/L)	
	48-h Acute	NU-536	EC_{50} > 24.4 mg/L (0% immobilization)	Not toxic up to the highest concentration tested	2398978
	48-h Acute	TJ-537	EC_{50} > 0.355 mg/L (45% immobilization)	Less than 50% mortality up to the highest concentration tested, which is around the limit of solubility under the test conditions (0.4 mg/L)	2398977
	21-d Chronic	Cyclaniliprole	$NOEC_{reproduction}$ = 0.010 mg a.i./L (nominal; 11.2% inhibition at 0.015 mg a.i./L)	No classification	2398981
Midge, *Chironomus riparius*	48-h Acute, water only	Cyclaniliprole	EC_{50} > 0.0533 mg a.i./L (45% immobilization)	Very highly toxic, based on an EC_{50} set at 0.0533 mg a.i./L	2398980
	21-d Chronic, spiked sediment	Cyclaniliprole	Cyclaniliprole did not appear to have a significant impact on the development rate or sex ratio profile of the midge at a sediment concentration of 0.061 mg a.i./kg	No classification	2398987
Rainbow trout, *Oncorhynchus mykiss*	96-h Acute	Cyclaniliprole	LC_{50} > 0.195 mg a.i./L (0% mortality)	Not toxic up to the limit of solubility in water under the test conditions	2398965
	96-h Acute	Cyclaniliprole 50SL (End-Use Product)	LC_{50} = 361 mg product/L (nominal) (15.3 mg a.i./L, mean measured)	The end-use product is not more toxic than cyclaniliprole alone.	2399049
Bluegill sunfish, *Lepomis macrochirus*	96-h Acute	Cyclaniliprole	LC_{50} > 0.143 mg a.i./L (0% mortality)	Not toxic up to the highest concentration tested which approaches the limit of solubility in water	2398971
Carp, *Cyprinus carpio*	96-h Acute	Cyclaniliprole	LC_{50} > 0.63 mg a.i./L (0% mortality)	Not toxic up to the limit of solubility in dilution water under the test conditions	2398967
Fathead minnow, *Pimephales promelas*	33-d Early-life stage; exposure from 5 d pre-hatch to	Cyclaniliprole	NOEC = 0.212 mg a.i./L (highest concentration tested) (no treatment-	No classification Not toxic up to the limit of solubility in water under the test	2398974

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	PMRA#
	28 d post-hatch		related effects)	conditions	
Green alga, *Pseudokirchneriella subcapitata*	96-h Acute	Cyclaniliprole	EC_{50} > 0.152 mg a.i./L (11.9% and 12% reductions in cell density and yield, respectively)	No classification Not toxic up to the limit of solubility in water under the test conditions	2398982
	96-h Acute	Cyclaniliprole 50SL (End-Use Product)	$EC_{50\ \text{cell density and yield}}$ = approximately 1000 mg product/L (approximately 48.3 mg a.i./L)	No classification The end-use product is not more toxic than cyclaniliprole alone.	2399051
Blue-green alga, *Anabaena* sp.	96-h Acute	Cyclaniliprole	EC_{50} > 0.15 mg a.i./L (8.3% reduction in growth rate)	No classification Not toxic up to the limit of solubility in water under the test conditions	2398985
Diatom, *Navicula pelliculosa*	96-h Acute	Cyclaniliprole	EC_{50} > 0.099 mg a.i./L (6.2-13% stimulation)	No classification Not toxic up to the highest concentration tested	2398984
Vascular plant, duckweed, *Lemna gibba*	7-d Dissolved	Cyclaniliprole	EC_{50} > 0.195 mg a.i./L (no treatment-related inhibition)	No classification Not toxic up to the limit of solubility in water under the test conditions	2398989
Marine/estuarine species					
Crustacean, mysid shrimp, *Americamysis bahia*	96-h Acute	Cyclaniliprole	LC_{50} > 0.2 mg a.i./L (0% mortality)	Not toxic up to the limit of solubility in water	2398964
Mollusk, Eastern oyster, *Crassostrea virginica*	96-h Acute	Cyclaniliprole	EC_{50} = 0.023 mg a.i./L (shell deposition)	Very highly toxic	2398962
Sheepshead minnow, *Cyprinodon variegatus*	96-h Acute	Cyclaniliprole	LC_{50} > 0.16 mg a.i./L (0% mortality)	Not toxic up to the limit of solubility in water under the test conditions	2398969
Marine diatom, *Skeletonema grethae*	96-h Acute	Cyclaniliprole	EC_{50} > 0.122 mg a.i./L (no treatment-related inhibition)	No classification Not toxic up to the highest concentration tested which approaches the limit of solubility in water	2398983

[1] U.S. EPA classification, where applicable

Table 19 Screening Level Risk Assessment of Cyclaniliprole for Aquatic Species

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	Level of Concern
Freshwater species					
Invertebrate, *Daphnia magna*	Acute	EC_{50}/2: 0.0404	0.0368	0.9	Not exceeded
	Chronic	NOEC: 0.010	0.0368	**3.7**	Exceeded
Sediment dwelling invertebrate, *Chironomus riparius*	Acute	EC_{50}/2: 0.0267[1]	0.0368	**1.4**	Exceeded
Fish	Acute	LC_{50}/10: > 0.063	0.0368	< 0.6	Not exceeded
	Early-life stage	NOEC: 0.212	0.0368	0.2	Not exceeded
Amphibians	Acute	LC_{50}/10: > 0.063	0.1962	< 3.1	Based on the relatively low risk quotient and 0% mortality up to the limit of solubility under the conditions of the test, a risk to amphibians is not expected.
	Chronic	NOEC: 0.212	0.1962	0.9	Not exceeded
Algae	Acute	EC_{50}/2: > 0.076	0.0368	< 0.5	Not exceeded
Vascular plants	Dissolved	EC_{50}/2: > 0.0975	0.0368	< 0.4	Not exceeded
Marine/estuarine species					
Crustaceans	Acute	LC_{50}/2: > 0.1	0.0368	< 0.4	Not exceeded
Mollusks	Acute	EC_{50}/2: 0.0115	0.0368	**3.2**	Exceeded
Fish	Acute	LC_{50}/10: > 0.016	0.0368	< 2.3	Based on the relatively low risk quotient and 0% mortality up to the limit of solubility under the conditions of the test, a risk to marine or estuarine fish is not expected.
Algae	Acute	EC_{50}/2: > 0.061	0.0368	< 0.6	Not exceeded

[1]As almost 50% immobilization (45%) was observed at the highest test concentration of 0.0533 mg a.i./L, a conservative estimate of the EC_{50} of 0.0533 mg a.i./L divided by an uncertainty factor of 2 was used for risk assessment.

Table 20 Screening Level Risk Assessment of Cyclaniliprole 50SL Insecticide for Aquatic Species

Organism	Exposure	Endpoint value (mg a.i./L)	EEC (mg a.i./L)	RQ	Level of Concern
Freshwater species					
Invertebrates	Acute	EC_{50}/2: 0.03695	0.0368	**1.0**	Exceeded
Fish	Acute	LC_{50}/10: 1.53	0.0368	< 0.1	Not exceeded
Amphibians	Acute	LC_{50}/10: 1.53	0.1962	0.1	Not exceeded
Algae	Acute	EC_{50}/2: 24.15	0.0368	< 0.1	Not exceeded

Table 21 Screening Level Risk Assessment of Cyclaniliprole Transformation Products for Aquatic Species

Organism	Exposure	Endpoint value (mg/L)	EEC (mg/L)	RQ	Level of Concern
NK-1375					
Freshwater invertebrates	Acute	EC_{50}/2: > 0.027	0.0346	< 1.3	Based on the risk quotient close to 1, and 0% immobilization at the highest concentration tested which approached the limit of solubility in water, a risk to freshwater invertebrates is not expected.
NU-536					
Freshwater invertebrates	Acute	EC_{50}/2: > 12.2	0.0308	< 0.1	Not exceeded
TJ-537					
Freshwater invertebrates	Acute	EC_{50}/2: > 0.178	0.0289	< 0.2	Not exceeded

Table 22 Risk Quotients for Aquatic Organisms Determined for Drift of Cyclaniliprole

Organism (exposure)	Endpoint (µg a.i./L)	Refined EEC (mg a.i./L)	RQ	Level of Concern
Freshwater species				
Daphnia magna (Acute,	EC_{50}/2 = 0.03695 mg a.i./L	Early season airblast appl. (74% drift): 0.0272 mg a.i./L	0.7	Not exceeded

Organism (exposure)	Endpoint (µg a.i./L)	Refined EEC (mg a.i./L)	RQ	Level of Concern
48 hours, Cyclaniliprole 50SL Insecticide)		Late season airblast appl. (59% drift): 0.0217 mg a.i./L	0.6	Not exceeded
Daphnia magna (Chronic; 21 days, technical cyclaniliprole)	NOEC = 0.01 mg a.i./L	Early season airblast appl. (74% drift): 0.0272 mg a.i./L	**2.7**	Exceeded
		Late season airblast appl. (59% drift): 0.0217 mg a.i./L	**2.2**	Exceeded
Midge, *Chironomus riparius* (Acute, 48 hours, technical cyclaniliprole)	$EC_{50}/2$ = 0.0267 mg a.i./L	Early season airblast appl. (74% drift): 0.0272 mg a.i./L	**1.0**	Exceeded
		Late season airblast appl. (59% drift): 0.0217 mg a.i./L	0.8	Not exceeded
Marine species				
Eastern oyster, *Crassostrea virginica* (Acute, 96 hours, technical cyclaniliprole)	$EC_{50}/2$ = 0.0115 mg a.i./L	Early season airblast appl. (74% drift): 0.0272 mg a.i./L	**2.4**	Exceeded
		Late season airblast appl. (59% drift): 0.0217 mg a.i./L	**1.9**	Exceeded

Table 23 Risk Quotients for Aquatic Organisms as Determined for Runoff of Cyclaniliprole in Water Bodies 80 cm Deep

Organism (exposure)	Endpoint (mg a.i./L)	EEC 90th percentile concentrations[1] (time-frame)	RQ	Level of Concern
Freshwater species				
Daphnia magna (Acute, 48 hours, Cyclaniliprole 50SL Insecticide)	$EC_{50}/2$ = 0.03695 mg a.i./L	0.01 mg/L (peak)	0.3	Not exceeded
Daphnia magna (Chronic; 21 days, technical cyclaniliprole)	NOEC = 0.01 mg a.i./L	0.008 mg/L (21-d)	0.8	Not exceeded

Organism (exposure)	Endpoint (mg a.i./L)	EEC 90th percentile concentrations[1] (time-frame)	RQ	Level of Concern
Midge, *Chironomus riparius* (Acute, 48 hours, technical cyclaniliprole)	$EC_{50}/2$ = 0.0267 mg a.i./L	0.01 mg/L (peak)	0.4	Not exceeded
Marine species				
Eastern oyster, *Crassostrea virginica* (Acute, 96 hours, technical cyclaniliprole)	$EC_{50}/2$ = 0.0115 mg a.i./L	0.0095 mg/L (96-h)	0.8	Not exceeded

[1] Based on modelling of cyclaniliprole combined with transformation product NK-1375. The highest EECs in 80 cm were chosen, and these were from a scenario for the Atlantic region for use on various vegetables and small fruits (4 × 60 g a.i./ha at 5-d interval).

Table 24 Toxic Substances Management Policy Considerations – Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Cyclaniliprole Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	Representative half-lives: 1138-1728 days
	Water	Half-life ≥ 182 days	Representative half-lives of 67 to 100 days in the water phase of aerobic and anaerobic water-sediment systems. Total system half-lives range from 495 to 854 days in aerobic and anaerobic water sediment systems.
	Sediment	Half-life ≥ 365 days	Half-lives in the sediment phase of aerobic and anaerobic water-sediment systems could not be calculated because cyclaniliprole concentrations in sediment generally increased until study termination. Total system half-lives range from 495 to 854 days in aerobic and anaerobic water sediment systems.
	Air	Half-life ≥ 2 days or evidence of long range transport	Volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (2.4×10^{-6} Pa at 25°C) and Henry's law constant (9.5×10^{-8} atm m^3/mol at 20°C).

TSMP Track 1 Criteria	TSMP Track 1 Criterion value	Cyclaniliprole Endpoints
Bioaccumulation[4]	Log $K_{OW} \geq 5$	2.0-2.8
	BCF ≥ 5000	Whole fish steady state BCF: 48-95 Whole fish steady state BCF normalised to 5% lipid content: 193-374 Whole fish kinetic BCF: 87.8-202
	BAF ≥ 5000	Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?		No, does not meet 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 judgement, 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]Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, log K_{ow}).

Table 25 List of Supported Uses of Cyclaniliprole 50SL Insecticide. See label for complete use directions.

Pests	Use Pattern
Crop Group 11-09: Pome Fruit	
Controls: codling moth, obliquebanded leafroller, oriental fruit moth, threelined leafroller Suppresses: apple maggot, plum curculio, western flower thrips	Rate: 1.2-1.6 L product/ha Minimum re-application interval: 10 days Maximum number of applications/year: 5 Ground application only Maximum rate per year: 6 L/ha
Crop Group 12-09: Stone Fruit	
Controls: obliquebanded leafroller, oriental fruit moth, peach twig borer, spotted wing drosophila, threelined leafroller, walnut husk fly, western cherry fruit fly Suppresses: omnivorous leafroller, plum curculio, western flower thrips	Rate: 1.2-1.6 L product/ha Minimum re-application interval: 7 days Maximum number of applications/year: 5 Ground application only Maximum rate per year: 6 L/ha
Crop Subgroup 13-07F: Small Fruit, Vine Climbing	
Controls: grape berry moth, spotted wing drosophila Suppresses: omnivorous leafroller, western flower thrips	Rate: 1.2-1.6 L product/ha Minimum re-application interval: 7 days Maximum number of applications/year: 3 Ground application only Maximum rate per year: 4.8 L/ha

Crop Group 14-11: Tree Nuts	
Controls: codling moth, peach twig borer, walnut husk fly, obliquebanded leafroller, threelined leafroller	Rate: 1.2-1.6 L product/ha; use the high rate for codling moth Minimum re-application interval: 10 days Maximum number of applications/year: 5 Ground application only Maximum rate per year: 6 L/ha
Crop Group 4-13: Leafy Vegetables **Crop Group 5-13: Brassica Head and Stem Vegetables**	
Controls: beet armyworm, bertha armyworm, cabbage looper, diamondback moth, imported cabbageworm	Rate: 0.8-1.2 L product/ha Minimum re-application interval: 5 days Maximum number of applications/year: 6 Ground or aerial application Maximum rate per year: 4.8 L/ha
Controls: dipteran leafminers (*Liriomyza* spp.) Suppresses: western flower thrips, whiteflies	Rate: 1.2 L product/ha Minimum re-application interval: 5 days Maximum number of applications/year: 6 Ground or aerial application Maximum rate per year: 4.8 L/ha
Crop Group 8-09: Fruiting Vegetables	
Controls: beet armyworm, bertha armyworm, cabbage looper, Colorado potato beetle, fall armyworm	Rate: 0.8-1.2 L product/ha Minimum re-application interval: 5 days Maximum number of applications/year: 4 Ground or aerial application Maximum rate per year: 4.8 L/ha
Controls: dipteran leafminers (*Liriomyza* spp.) Suppresses: western flower thrips, whiteflies	Rate: 1.2 L product/ha Minimum re-application interval: 5 days Maximum number of applications/year: 4 Ground or aerial application Maximum rate per year: 4.8 L/ha
Crop Group 9: Cucurbit Vegetables	
Controls: beet armyworm, bertha armyworm, cabbage looper	Rate: 0.8-1.2 L product/ha Minimum re-application interval: 5 days Ground or aerial application Maximum number of applications/year: 4 Maximum rate per year: 4.8 L/ha

Controls: dipteran leafminers (*Liriomyza* spp.) Suppresses: western flower thrips, onion thrips, whiteflies	Rate: 1.2 L product/ha Minimum re-application interval: 5 days Ground or aerial application Maximum number of applications/year: 4 Maximum rate per year: 4.8 L/ha

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

Cyclaniliprole is a new active ingredient which is concurrently being registered in Canada and the United States. The MRLs proposed for cyclaniliprole in Canada are the same as corresponding tolerances to be promulgated in the United States.

Once established, the American tolerances for cyclaniliprole will be listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide.

Currently, there are no Codex MRLs[9] listed for cyclaniliprole in or on any commodity on the Codex Alimentarius Pesticide Residues in Food website.

Table 1 compares the MRLs proposed for cyclaniliprole in Canada with corresponding American tolerances and Codex MRLs[10]. American tolerances are listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide. A listing of established Codex MRLs is available on the Codex Alimentarius Pesticide Residues in Food website, by pesticide or 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)
Crop Group 4-13 (Leafy Vegetables)	15	15	Not Established
Crop Group 5-13 (*Brassica* Head and Stem Vegetable Group)	1	1	Not Established
Crop Group 8-09 (Fruiting Vegetables)	0.2	0.2	Not Established
Crop Group 9 (Cucurbit Vegetables)	0.15	0.15	Not Established
Crop Group 11-09 (Pome Fruits)	0.3	0.3	Not Established

9 The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)	Codex MRL (ppm)
Crop Group 12-09 (Stone Fruits)	1	1	Not Established
Crop Subgroup 13-07F (Small fruits vine climbing, except fuzzy kiwifruit)	0.8	0.8	Not Established
Crop Group 14-11 – (Tree Nuts)	0.03	0.03	Not Established
Meat of cattle, goats, horses and sheep	0.01	0.01	Not Established
Meat byproducts and fat of cattle, goats, horses and sheep	0.015	0.015	Not Established
Milk	0.015	0.015	Not Established

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA#	Reference
2398866	2014, Part 2 Chemistry Requirements for Registration of a Technical Grade of Active Ingredient, DACO: 2.1,2.10,2.2,2.3,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9
2398867	2014, Product Chemistry Studies for Technical Cyclaniliprole (IKI-3106) EPA 61 Series, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.13.2,IIA 1.8.1,IIA 1.8.2,IIA 2.5.2.2,IIA 2.5.2.4 CBI
2398868	2013, Product Chemistry Studies for Technical Cyclaniliprole (IKI-3106) - SERIES 62 -, DACO: 2.12.1,2.12.2,2.13.1,2.13.3,IIA 1.11.1,IIA 1.11.2,IIA 1.9.2,IIA 4.2.1 CBI
2398869	2012, Product Chemistry Studies for Technical Cyclaniliprole (IKI-3106) - SERIES 63 -, DACO: 2.12.1,2.12.2,2.13.2,2.14.1,2.14.10,2.14.11,2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7,2.14.8,2.14.9,2.16,8.2.3.2,IIA 2.1.1,IIA 2.1.2,IIA 2.11.1,IIA 2.12,IIA 2.13,IIA 2.15,IIA 2.16,IIA 2.17.1,IIA 2.17.2,IIA 2.2,IIA 2.3.1,IIA 2.4.1,IIA 2.4.2,IIA 2.5.1.1,IIA 2.5.1.2,IIA 2.5.1.3,IIA 2.5.1.4,IIA 2.5.1.6,IIA 2.6,IIA 2.7,IIA 2.8.1,IIA 2.9.5
2574848	2015, Amendment 1 - Product Chemistry Studies for Technical Cyclaniliprole (IKI-3106) EPA 61 Series, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,2.13.2,IIA 1.8.1,IIA 1.8.2,IIA 2.5.2.2,IIA 2.5.2.4 CBI
2574849	2015, Amendment 1 - Product Chemistry Studies for Technical Cyclaniliprole (IKI-3106) - Series 62 -, DACO: 2.12.1,2.12.2,2.13.1,2.13.3,IIA 1.11.1,IIA 1.11.2,IIA 1.9.2,IIA 4.2.1 CBI
2574851	2015, IKI-3106: Five-Batch Analysis, DACO: 2.13.3,IIA 1.11.1 CBI
2577382	2015, Revision of Materials used to Produce Technical Cyclaniliprole - Alternate starting material, DACO: 2.11.2,2.11.3 CBI
2398874	2012, IKI-3106 and NK-1375: Validation of an Analytical Method for the Determination of IKI-3106 and Its Metabolite (NK-1375) in Soil, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6
2398875	2013, Independent Laboratory Validation of Method 1-605: "Analysis of IKI-3106 and Metabolite NK-1375 in/on Soil by LC-MS/MS", DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6
2398876	2011, IKI-3106 Validation of Methodology for the Determination of Residues of IKI-3106 in Dechlorinated Tap Water and OECD Medium, DACO: 8.2.2.3,IIA 4.5
2398877	2013, IKI-3106 and Metabolites (NK-1375, NSY-137, TJ-537 and NU-536): Validation of Methodology for the Determination of Residues in Drinking Water and Surface Water, DACO: 8.2.2.3,IIA 4.5
2398878	2014, Development and Validation of the Analytical Method for the Determination of IKI-3106 and Its Metabolites NK-1375, NSY-137, TJ-537 and NU-536 in Drinking Water and Surface Water, DACO: 8.2.2.3,IIA 4.5
2398857	2014, OECD Dossier Annex II: Active Substance Document M-II: Tier II Summary Section 1, DACO: 12.7,Document M
2398858	2014, OECD Dossier Annex II: Technical Cyclaniliprole Document M-II: Tier II Summary (Methods) Section 2, DACO: 12.7,Document M PMRA Document
2399042	2014, Cyclaniliprole 50SL Insecticide PART 3.1 Product Identification , DACO: 3.1.1,3.1.2,3.1.3,3.1.4,IIIA 1.1,IIIA 1.2.1,IIIA 1.3
2399043	2014, Product Chemistry Studies for Cyclaniliprole 50SL - Series 61 -, DACO: 3.2.2,3.2.3,IIIA 1.4.5.1,IIIA 1.4.5.2 CBI
2399084	2013, Product Chemistry Studies for Cyclaniliprole 50SL (IKI-3106) - Series 63 -, DACO: 3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2,3.5.3,3.5.6,3.5.7,3.5.8,3.5.9,IIIA 2.1,IIIA 2.11,IIIA 2.12,IIIA 2.13,IIIA 2.2.1,IIIA 2.2.2,IIIA 2.3.2,IIIA 2.4.1,IIIA 2.5.1,IIIA 2.6.1,IIIA 2.7.5
2399089	2014, Product Chemistry Studies for Cyclaniliprole 50SL - Series 62 -, DACO: 3.3.1,3.3.2,3.4.1,IIIA 1.4.2,IIIA 5.2.1 CBI
2434792	2014, Petition for (CBI removed) (CAS RN 67-68-5) to Establish an Exemption from the Requirement for a tolerance in accordance with 40 CFR¿¿180.920 for Post-Emergence Pre-Harvest Use in Cyclaniliprole 50 SL Formulations, DACO: 3.2.1 CBI

PMRA#	Reference
2434793	2014, Compilation of References for the Petition for (CBI removed) (CAS RN 67-68-5), DACO: 3.2.1 CBI
2399029	2014, OECD Dossier Annex III: Plant Protection Product Document M-III: Tier II Summary (Phys Chem) Section 1, DACO: 12.7,Document M
2399030	2014, OECD Dossier Annex III: Plant Protection Product Document M-III: Tier II Summary (Methods) Section 2, DACO: 12.7,Document M

2.0 Human and Animal Health

PMRA#	Reference
2004944	AHETF, 2010. Agricultural Handler Exposure Scenario Monograph: Open Cab Airblast Application.ofLiquid Sprays. Report Number AHE1006. December 14, 2010.
2115788	Agricultural Reentry Task Force (ARTF). 2008. Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients. Submission #2006-0257.
2399186	2013, IKI-3106 50SL: In vivo Dermal Absorption Study in the Male Rat, DACO: 5.8,IIIA 7.6.1
2399187	2013, IKI-3106 50SL: In vitro Dermal Absorption Study Using Rat Skin, DACO: 5.8,IIIA 7.6.2
2399188	2013, IKI-3106 50SL: In vitro Dermal Absorption Study Using Human Skin, DACO: 5.8,IIIA 7.6.2
2399189	2014, Dislodgeable Foliar Residue Study IKI-3106 on Grapes - USA in 2013, DACO: 5.9,IIIA 7.7.1
2399190	2014, Dislodgeable Foliar Residue Study IKI-3106 on Apples - USA in 2013, DACO: 5.9,IIIA 7.7.1
2399191	2014, Dislodgeable Foliar Residue Study IKI-3106 on Squash - USA in 2013, DACO: 5.9,IIIA 7.7.1
2398926	2013, IKI-3106 Metabolism in Lettuce, DACO: 6.3,IIA 6.2.1
2398927	2013, IKI-3106 Metabolism in Potatoes, DACO: 6.3,IIA 6.2.1
2398928	2013, IKI-3106 Metabolism in Apples, DACO: 6.3,IIA 6.2.1
2398929	2013, IKI-3106 Metabolism in Laying Hens, DACO: 6.2,IIA 6.2.2
2398930	2013, IKI-3106 Metabolism in the Lactating Goat, DACO: 6.2,IIA 6.2.3
2399090	2014, IKI-3106 and NK-1375: Validation of Methodology for the Determination of Residues of IKI-3106 and NK-1375 in Grape, Wine, Peaches, Oilseed Rape Seeds and Dry Beans, DACO: 7.2.1,7.2.2,7.2.3,7.2.4,7.2.5,IIIA 5.3.1
2399093	2013, Independent Laboratory Validation of Ishihara Sangyo Kaisha (ISK) Residue Analytical Method for the Determination of IKI-3106 and Its Metabolite NK-1375 in Almonds, Apples, Lettuce, and Wheat, DACO: 7.2.1,7.2.2,7.2.3,7.2.4,7.2.5,IIIA 5.3.1
2399099	2014, IKI-3106: Radiovalidation of the Extraction Efficiency of the Residue Analytical Method for Lettuce Plants, DACO: 7.2.1,7.2.2,7.2.3,7.2.4,7.2.5,IIIA 5.3.1
2399192	2013, Interim Report IKI-3106 and Metabolite NK-1375: Storage Stability in a Range of Crop Matrices for Periods of up to 18 Months, DACO: 7.3,IIIA 8.1.1
2399193	2014, Magnitude of Residues of IKI-3106 on Almonds and Pecans - USA in 2012, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1
2399194	2014, Magnitude of Residues of IKI-3106 on Cucurbits - USA & Canada in 2013, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1
2399195	2014, Magnitude of Residues of IKI-3106 on Leafy Brassicas - USA and Canada in 2012, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1
2399196	2014, Magnitude of Residues of IKI-3106 on Grapes - USA & Canada in 2013, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1
2399197	2014, Magnitude of Residues of IKI-3106 on Lettuce and Spinach USA & Canada in 2012, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1
2399198	2014, Magnitude of Residues of IKI-3106 on Pome Fruit - USA and Canada in 2013, DACO: 7.4.1,7.4.2,7.4.6,IIIA 8.3.1
2399203	2013, IKI-3106 50SL (IBE 4064) Residue Study (at Harvest and Processing) with IKI-3106 50SL (IBE 4064) Applied to Wine Grapes in Northern and Southern Europe 2012, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,8.4.1,IIIA 8.3.1,IIIA 8.5.1

PMRA#	Reference
2399206	2014, Magnitude of Residues of IKI-3106 on Stone Fruit - USA and Canada in 2013, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,8.4.1,IIIA 8.3.1,IIIA 8.5.1
2399207	2014, Magnitude of Residues of IKI-3106 on Fruiting Vegetables - USA and Canada in 2012, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,8.4.1,IIIA 8.3.1,IIIA 8.5.1
2399208	2013, Magnitude of Residues of IKI-3106 on Apples - USA and Canada in 2012, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,8.4.1,IIIA 8.3.1,IIIA 8.5.1,IIIA 8.5.2
2399209	2013, IKI-3106: Residue Transfer Study (Feeding Study) in Dairy Cows, DACO: 6.2,7.5,7.6,IIIA 8.4.2
2399211	2013, IKI-3106 Accumulation in Confined Rotational Crops, DACO: 7.4.3,7.4.4,IIIA 8.6
2399212	2013, IKI-3106 50SL (IBE4064) Crop Rotation Residue Study with IKI-3106 50SL (IBE4064) Applied to Outdoor Tomato and Outdoor Peppers in Northern And Southern Europe in 2012, DACO: 7.4.3,7.4.4,IIIA 8.6
2399213	2013, Field Accumulation of IKI-3106 in Rotational Crop Wheat - USA in 2012, DACO: 7.4.3,7.4.4,IIIA 8.6
2444535	2013, Independent Laboratory Validation of the Analytical Method for the Determination of IKI-3106 and Metabolites in Animal Tissues, DACO: 171 - 4a,171 - 4c,171 - 4m,171-4a-4b,171-4c-4d,7.2.2,7.2.3A,860.1300,860.1340,860.1360,IIA 4.2.6,IIIA 5.3.1,b,d
2444536	2014, IKI-3106: Radiovalidation of the Extraction Efficiency of the Residue Analytical Method for Animal Tissues, DACO: 7.2.2,7.2.3B
2444537	2014, Final Report IKI-3106 and Metabolite NK-1375: Storage Stability in a Range of Crop Matrices for Periods of up to 18 Months, DACO: 7.3
2398882	2013, IKI-3106 Metabolism in rats, DACO: 4.5.9,IIA 5.1.1,IIA 5.1.2,IIA 5.1.3
2398884	2013, IKI-3106 Technical: 4 week Dietary Immunotoxicity Study in the Female CD-I Mouse, DACO: 4.2.9,4.3.8,4.4.5,4.5.8,4.8,IIA 5.10
2398885	2011, IKI-3106: Acute Oral Toxicity to the Rat (Acute Toxic Class Method), DACO: 4.2.1,IIA 5.2.1
2398886	2012, NK-1375, A Degradation Product of IKI-3106: Acute Oral Toxicity to the Rat (Acute Toxic Class Method), DACO: 4.2.1,IIA 5.2.1
2398887	2011, IKI-3106: Acute Dermal Toxicity to the Rat, DACO: 4.2.2,IIA 5.2.2
2398888	2011, IKI-3106 TGAI: Acute 4 hour (Nose Only) Inhalation Study in the Rat, DACO: 4.2.3,IIA 5.2.3
2398890	2011, IKI-3106 TGAI: Skin Irritation Study in Rabbits, DACO: 4.2.5,IIA 5.2.4
2398891	2011, IKI-3106 TGAI: Eye Irritation Study in Rabbits, DACO: 4.2.4,IIA 5.2.5
2398894	2011, IKI-3106 TGAI: Skin Sensitization Study in Mice -Local Lymph Node Assay, DACO: 4.2.6,IIA 5.2.6
2398895	2011, A Skin Sensitization Study of IKI-3106 TGAI in Guinea Pigs (Maximization Test), DACO: 4.2.6,IIA 5.2.6
2398896	2010, IKI-3106 TGAI: Repeated Dose 28-day Oral Toxicity Study in Rats, DACO: 4.3.3,IIA 5.3.1
2398897	2013, IKI-3106 TGAI: Repeated Dose 28-day Oral Toxicity Study in Dogs, DACO: 4.3.3,IIA 5.3.1
2398898	2011, IKI-3106 TGAI: Repeated Dose 90-day Oral Toxicity Study in Rats, DACO: 4.3.1,IIA 5.3.2
2398900	2012, IKI-3106 Technical Preliminary Carcinogenicity Study by Dietary Administration to the CD-I Mouse for 13 weeks, DACO: 4.3.1,IIA 5.3.2
2398904	2013, IKI-3106 TGAI: Repeated Dose 90-day Oral Toxicity Study in Dogs, DACO: 4.3.2,IIA 5.3.3
2398905	2013, IKI-3106 TGAI: Repeated Dose 1-year Oral Toxicity Study in Dogs, DACO: 4.3.2,IIA 5.3.4
2398908	2013, IKI-3106 Technical: Toxicity Study by Dermal Administration to Sprague-Dawley Rats For 4 weeks, DACO: 4.3.5,IIA 5.3.7
2398909	2011, IKI-3106 TGAI: Bacterial Reverse Mutation Test, DACO: 4.5.4,IIA 5.4.1
2398910	2011, IKI-3106 TGAI: Chromosome Aberration Test in Cultured Mammalian Cells, DACO: 4.5.6,IIA 5.4.2
2398911	2012, IKI-3106 TGAI: Gene Mutation Test in Mouse Lymphoma Cells, DACO: 4.5.5,IIA 5.4.3
2398912	2011, IKI-3106 TGAI: Micronucleus Test in Mice, DACO: 4.5.7,IIA 5.4.4
2398913	2013, IKI-3106 TGAI: Repeated Dose 1-year Oral Toxicity Study in Rats, DACO: 4.4.1,4.4.4,IIA 5.5.1
2398914	2013, IKI-3106 TGAI: Carcinogenicity Study in Rats, DACO: 4.4.2,4.4.4,IIA 5.5.2

PMRA#	Reference
2398915	2013, IKI-3106 Technical: Carcinogenicity Study by Dietary Administration to the CD-I Mouse for 78 WEEKS, DACO: 4.4.3,IIA 5.5.3
2398916	2012, TWO-GENERATION REPRODUCTIVE TOXICITY STUDY OF IKI-3106 TGAI IN RATS, DOSE-RANGE FINDING STUDY, DACO: 4.5.1,IIA 5.6.1
2398917	2013, TWO-GENERATION REPRODUCTIVE TOXICITY STUDY OF IKI-3106 TGAI IN RATS, DACO: 4.5.1,IIA 5.6.1
2398918	2012, IKI-3106 TGAI: DOSE RANGE-FINDING TERATOGENICITY STUDY IN RATS, DACO: 4.5.2,IIA 5.6.10
2398919	2012, IKI-3106 TGAI: TERATOGENICITY STUDY IN RATS, DACO: 4.5.2,IIA 5.6.10
2398920	2011, IKI-3106 TGAI: DOSE RANGE-FINDING TERATOGENICITY STUDY IN RABBITS, DACO: 4.5.2,IIA 5.6.10
2398922	2013, IKI-3106 TGAI: TERATOGENICITY STUDY IN RABBITS, DACO: 4.5.3,IIA 5.6.11
2398923	2012, IKI-3106 TECHNICAL: NEUROTOXICITY STUDY BY ORAL GAVAGE ADMINISTRATION TO SPRAGUE-DAWLEY RATS FOLLOWED BY A 14-DAY OBSERVATION PERIOD, DACO: 4.5.12,IIA 5.7.1
2398924	2012, IKI-3106 TECHNICAL: NEUROTOXICITY STUDY BY DIETARY ADMINISTRATION TO SPRAGUE-DAWLEY RATS FOR 13 WEEKS, DACO: 4.5.13,IIA 5.7.4
2398925	2012, NK-1375, A Degradate of IKI-3106 Bacterial Reverse Mutation Test, DACO: 4.8,IIA 5.8
2444521	2014, Waiver Request for a 90-Day Inhalation Toxicity Study with Cyclaniliprole Technical, DACO: 4.3.6
2444522	2007, Validation of Neuropathology Procedures Neurotoxicity Study by Oral Gavage Administration of Acrylamide or Triethyltin Bromide to Male CD Rats, DACO: 4.5.12,4.5.13
2444523	2011, Further Validation of Neurotoxicity Procedures Following Oral Gavage Administration of D-Amphetamine or Di-Isopropyl Fluoro-Phosphate to CD Rats, DACO: 4.5.12,4.5.13
2502018	2013, IKI-3106: Biliary excretion in dogs, DACO: 4.5.9
2516522	2015, Historical Control Data Submission, DACO: 4.5.1
2521792	2015, Response to Request for Historical Control Data IKI-3106 TGAI: Repeated Dose 1-year Oral Toxicity Study in Dogs, DACO: 4.3.2,IIA 5.3.4
2523311	2015, Historical Control Data Submission, DACO: 4.5.1
2399177	2012, IKI-3106 50SL: Acute Oral Toxicity to the Rat (Acute Toxic Class Method), DACO: 4.6.1,IIIA 7.1.1
2399178	2012, IKI-3106 50SL: Acute Dermal Toxicity to the Rat, DACO: 4.6.2,IIIA 7.1.2
2399179	2013, IKI-3106 50SL: Acute (Four-Hour) Inhalation Study in Rats, DACO: 4.6.3,IIIA 7.1.3
2399180	2012, IKI-3106 TGAI 50SL: Skin Irritation Study in Rabbits, DACO: 4.6.5,IIIA 7.1.4
2399181	2012, IKI-3106 50SL: Eye Irritation Study in Rabbits, DACO: 4.6.4,IIIA 7.1.5
2399182	2012, IKI-3106 50SL: Skin Sensitization Study in Mice -Local Lymph Node Assay, DACO: 4.6.6,IIIA 7.1.6
2399183	2012, A Skin Sensitization Study of IKI-3106 50SL in Guinea Pigs (Buehler Test), DACO: 4.6.6,IIIA 7.1.6
2444534	2012, A Skin Sensitization Study of IKI-3106 50SL in Guinea Pigs (Buehler Test), DACO: 4.6.6

3.0 Environment

PMRA#	Reference
2398871	2010, IKI-3106 Hydrolysis in water, DACO: 8.2.3.2,IIA 2.9.1
2398872	2013, IKI-3106: Photodegradation in Water and Determination of the Quantum Yield, DACO: 8.2.3.3.2,IIA 2.9.2
2398874	2012, IKI-3106 AND NK-1375: Validation of an Analytical Method for the Determination of IKI-3106 and its Metabolite (NK-1375) in Soil, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6
2398876	2011, IKI-3106 Validation of Methodology for the Determination of Residues of IKI-3106 in Dechlorinated Tap Water and OECD Medium, DACO: 8.2.2.3,IIA 4.5

PMRA#	Reference
2398877	2013, IKI-3106 and metabolites (NK-1375, NSY-137, TJ-537 and NU-536): Validation of Methodology for the Determination of Residues in Drinking Water and Surface Water, DACO: 8.2.2.3,IIA 4.5
2398881	2013, IKI-3106 and Metabolites: Validation of Methodology for the Determination of Residues of IKI-3106 and Metabolites in Animal Tissues, DACO: 8.2.2.4,IIA 4.8
2398885	2011, IKI-3106: Acute oral toxicity to the rat (acute toxic class method), DACO: 4.2.1,IIA 5.2.1
2398886	2012, NK-1375, a degradation product of IKI-3106: Acute Oral Toxicity to the Rat (Acute Toxic Class Method), DACO: 4.2.1,IIA 5.2.1
2398916	2012, Two-Generation Reproductive Toxicity Study of IKI-3106 TGAI in Rats, Dose-Range Finding Study, DACO: 4.5.1,IIA 5.6.1
2398919	2012, IKI-3106 TGAI: Teratogenicity Study in Rats, DACO: 4.5.2,IIA 5.6.10
2398933	2013, [^{14}C]IKI-3106 – Aerobic Soil Metabolism and Degradation, DACO: 8.2.3.4.2,IIA 7.1.1
2398934	2013, [^{14}C]IKI-3106 – Aerobic Degradation in Four Soils, DACO: 8.2.3.4.2,IIA 7.1.1
2398936	2013, [^{14}C]IKI-3106 – Anaerobic Soil Metabolism and Degradation, DACO: 8.2.3.4.4,IIA 7.1.2
2398937	2011, IKI-3106 Soil photolysis, DACO: 8.2.3.3.1,IIA 7.1.3
2398941	2013, IKI-3106: Adsorption/desorption in five soils, DACO: 8.2.4.2,IIA 7.4.1
2398943	2013, NK-1375 (Metabolite of IKI-3106) Adsorption Coefficient, DACO: 8.2.4.2,IIA 7.4.2
2398945	2013, IKI-3106: Anaerobic Aquatic Metabolism, DACO: 8.2.3.5.5,8.2.3.5.6,IIA 7.8.2
2398946	2013, IKI-3106: Aerobic Aquatic Metabolism, DACO: 8.2.3.5.2,8.2.3.5.4,8.2.3.6,IIA 7.8.1,IIA 7.8.3
2398950	2013, IKI-3106 Acute Oral Toxicity (LD_{50}) to the Bobwhite quail, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
2398952	2014, IKI-3106 (TGAI): Canary (*Serinus canaria*) Oral Acute Toxicity Limit Test (LD_{50}), DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
2398954	2012, IKI-3106 Dietary Toxicity (LC_{50}) to the Bobwhite Quail, DACO: 9.6.2.4,9.6.2.5,IIA 8.1.2
2398956	2012, IKI-3106 Dietary Toxicity (LC_{50}) to the Mallard Duck, DACO: 9.6.2.4,9.6.2.5,IIA 8.1.2
2398958	2013, IKI-3106 Assessment To Determine The Effects On Reproduction In The Bobwhite Quail, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4
2398960	2013, IKI-3106: Assessment to Determine the Effects on Reproduction in the Mallard Duck, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4
2398962	2013, IKI-3106 TGAI: A 96-Hour Shell Deposition Test with the Eastern Oyster (*Crassostrea virginica*), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1
2398964	2013, A 96-hour Acute Toxicity Study of IKI-3106 TGAI in Mysid shrimp (*Americamysis bahia*), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1
2398965	2012, IKI-3106 Technical: Acute Toxicity to Rainbow Trout, DACO: 9.5.2.1,9.5.2.3,IIA 8.2.1.1
2398967	2011, Acute Toxicity Test of IKI-3106 TGAI with Carp (*Cyprinus carpio*), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
2398969	2012, IKI-3106 TGAI: A 96-Hour Flow-Through Acute Toxicity Test with the Sheepshead Minnow (*Cyprinodon variegatus*), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
2398971	2013, IKI-3106 TGAI Acute Toxicity To Bluegill Sunfish, DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
2398974	2013, An Early-life Stage Toxicity Study of IKI-3106 TGAI in Fathead minnow, DACO: 9.5.3.1,IIA 8.2.4
2398975	2013, IKI-3106 Bioconcentration in Bluegill Sunfish, DACO: 9.5.6,IIA 8.2.6.1
2398976	2011, Acute Immobilization Test of IKI-3106 TGAI with *Daphnia magna*, DACO: 9.3.2,IIA 8.3.1.1
2398977	2013, TJ-537 Acute Toxicity to *Daphnia magna*: IKI-3106 Related Study, DACO: 9.3.2,IIA 8.3.1.1
2398978	2013, NU-536 Acute Toxicity to *Daphnia magna*: IKI-3106 Related Study, DACO: 9.3.2,IIA 8.3.1.1
2398979	2013, NK-1375 Acute Toxicity to *Daphnia magna*: IKI-3106 Related Study, DACO: 9.3.2,IIA 8.3.1.1
2398980	2013, IKI-3106 (TGAI): Acute Toxicity to the Larval Phase of the Midge *Chironomus riparius*, DACO: 9.3.4,IIA 8.3.1.2
2398981	2013, Reproduction Test of IKI-3106 TGAI with *Daphnia magna*, DACO: 9.3.3,IIA 8.3.2.1

PMRA#	Reference
2398982	2012, IKI-3106 Technical: Algal Growth Inhibition Assay, DACO: 9.8.2,9.8.3,IIA 8.4
2398983	2013, IKI-3106 Technical Algal Growth Inhibition Assay (*Skeletonema grethae*), DACO: 9.8.2,9.8.3,IIA 8.4
2398984	2013, IKI-3106 Technical Algal Growth Inhibition Assay (*Navicula Pelliculosa*), DACO: 9.8.2,9.8.3,IIA 8.4
2398985	2013, IKI-3106 Technical Algal Growth Inhibition Assay – *Anabaena* sp., DACO: 9.8.2,9.8.3,IIA 8.4
2398987	2013, IKI-3106 Toxicity to the Sediment-Dwelling Phase of the Midge *Chironomus riparius*, DACO: 9.9,IIA 8.5.2
2398989	2012, IKI-3106 Technical Higher Plant (*Lemna*) Growth Inhibition Test, DACO: 9.8.5,IIA 8.6
2398991	2012, Final Report (2nd Original) Effects of IKI-3106 TGAI (Acute Contact and Oral) on Honey Bees (*Apis mellifera* L.) in the Laboratory, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2
2398993	2012, Final Report (2nd Original) Effects of IKI-3106 Technical on the Reproduction of the Collembola *Folsomia candida* in Artificial Soil with 5% Peat, DACO: 9.2.7,IIA 8.8.2.5
2398995	2013, IKI-3106 (TGAI) Predatory Mite (*Hypoaspis aculeifer*) Reproduction Test in Soil, DACO: 9.2.7,IIA 8.8.2.5
2398997	2011, Final Report (2nd Original) Acute Toxicity (14 Days) of IKI-3106 Technical to the Earthworm *Eisenia fetida* in Artificial Soil, DACO: 9.2.3.1,IIA 8.9.1
2398999	2012, Final Report (2nd Original) Effects of IKI-3106 Technical on Reproduction and Growth of Earthworms *Eisenia fetida* in Artificial Soil with 5% Peat, DACO: 9.2.3.1,IIA 8.9.2
2399049	2013, IKI-3106 50SL Acute Toxicity To Rainbow Trout, DACO: 9.5.4,IIIA 10.2.2.1
2399051	2013, IKI-3106 50SL Algal Growth Inhibition Assay, DACO: 9.8.2,9.8.3,IIIA 10.2.2.3
2399053	2012, Final Report (2nd Original) Effects of IKI-3106 50SL (Acute Contact and Oral) on Honey Bees (*Apis mellifera* L.) in the Laboratory, DACO: 9.2.8,IIIA 10.4.2.1,IIIA 10.4.2.2
2399054	2013, Final Report (2nd Original) Study on the Effect of IKI-3106 50SL on Honey Bees (*Apis mellifera* L.) under Field Conditions including Brood Assessments Field Test: Application after Bee Flight, DACO: 9.2.9,IIIA 10.4.5
2399059	2013, Final Report (2nd Original) Study on the Effect of IKI-3106 50SL on Honey Bees (*Apis mellifera* L.) under Field Conditions including Brood Assessments Field Test: Application After Bee Flight, DACO: 9.2.9,IIIA 10.4.5
2399062	2013, Final Report (2nd Original) Study on the Effect of IKI-3106 50SL on Honey Bees (*Apis mellifera* L.) under Field Conditions including Brood Assessments Field Test: Application during Bee Flight, DACO: 9.2.9,IIIA 10.4.5
2399068	2013, Final Report (2nd Original) Study on the Effect of IKI-3106 50SL on Honey Bee Brood (*Apis mellifera* L.) under Semi-Field Conditions Tunnel Test: Application after Bee Flight, DACO: 9.2.8,IIIA 10.4.7
2399070	2013, Final Report (2nd Original) Study on the Effect of IKI-3106 50SL on Honey Bee Brood (*Apis mellifera* L.) under Semi-Field Conditions Tunnel Test: Application After Bee Flight, DACO: 9.2.8,IIIA 10.4.7
2399073	2013, Final Report (2nd Original) Study on the Effect of IKI-3106 50SL on Honey Bee Brood (*Apis mellifera* L.) under Semi-Field Conditions Tunnel Test: Application after Bee Flight, DACO: 9.2.8,IIIA 10.4.7
2399075	2012, IKI-3106 50SL Acute Toxicity to *Typhlodromus pyri* in the Laboratory, DACO: 9.2.8,IIIA 10.5.1
2399076	2012, IKI-3106 50SL Acute Toxicity to *Aphidius rhopalosiphi* in the Laboratory, DACO: 9.2.8,IIIA 10.5.1
2399077	2013, Evaluation of the Effects of IKI-3106 50SL on the Parasitoid Wasp *Aphidius rhopalosiphi* in an Extended Laboratory/Aged Residue Study on Broad Bean, DACO: 9.2.8,IIIA 10.5.2
2399078	2013, Evaluation of the Effects of IKI-3106 50SL on the Rove Beetle *Aleochara bilineata* in an Extended Laboratory/Aged Residue Study in Soil, DACO: 9.2.8,IIIA 10.5.2
2399079	2013, Evaluation of the Effects of IKI-3106 50SL on the Ladybird Beetle *Coccinella septempunctata* in an Extended Laboratory/Aged Residue Study on Broad Bean, DACO: 9.2.8,IIIA 10.5.2

PMRA#	Reference
2399081	2012, Final Report (2nd Original) Acute Toxicity (14 Days) of IKI-3106 50SL to the Earthworm *Eisenia fetida* in Artificial Soil, DACO: 9.2.8,IIIA 10.6.2
2399082	2013, IKI-3106 50SL Seedling Emergence, DACO: 9.8.6,IIIA 10.8.1.1
2399083	2013, IKl-3106 50SL Vegetative Vigour, DACO: 9.8.6,IIIA 10.8.1.2
2399090	2014, IKI-3106 and NK-1375: Validation of Methodology for the Determination of Residues of IKI-3106 and NK-1375 in Grape, Wine, Peaches, Oilseed Rape Seeds and Dry Beans, DACO: 7.2.1,7.2.2,7.2.3,7.2.4,7.2.5,IIIA 5.3.1
2399093	2013, Independent Laboratory Validation of Ishihara Sangyo Kaisha (ISK) Residue Analytical Method for the Determination of IKI-3106 and its Metabolite NK-1375 in Almonds, Apples, Lettuce, and Wheat (Document Number: JSM0269), DACO: 7.2.1,7.2.2,7.2.3,7.2.4,7.2.5,IIIA 5.3.1
2399099	2014, IKI-3106: Radiovalidation of the Extraction Efficiency of the Residue Analytical Method for Lettuce Plants, DACO: 7.2.1,7.2.2,7.2.3,7.2.4,7.2.5,IIIA 5.3.1
2399177	2012, IKI-3106 50SL: Acute Oral Toxicity to the Rat (Acute Toxic Class Method), DACO: 4.6.1,IIIA 7.1.1
2399214	2013, Terrestrial Field Dissipation of IKI-3106 Applied to Bareground in Seven Springs, NC - USA 2011, DACO: 8.3.2.1,8.3.2.2,8.3.2.3,IIIA 9.2.1
2399215	2013, Terrestrial Field Dissipation of IKI-3106 Applied to Bareground in Kerman, CA - USA 2011, DACO: 8.3.2.1,8.3.2.2,8.3.2.3,IIIA 9.2.1
2399216	2013, Freezer Storage Stability of IKI-3106 in Soil, DACO: 8.3.2.1,8.3.2.2,8.3.2.3,IIIA 9.2.1
2399217	2014, Terrestrial Field Dissipation of IKI-3106 Applied to Bareground in North Rose, NY - USA 2012, DACO: 8.3.2.1,8.3.2.2,8.3.2.3,IIIA 9.2.1
2399218	2014, Terrestrial Field Dissipation of IKI-3106 Applied to Bareground in Ephrata, W A - USA 2012, DACO: 8.3.2.1,8.3.2.2,8.3.2.3,IIIA 9.2.1
2444535	2013, Independent laboratory validation of the analytical method for the determination of IKI-3106 and metabolites in animal tissues, DACO: 7.2.2,7.2.3A,860.1300,860.1340,860.1360,IIA 4.2.6,IIIA 5.3.1,b,d
2444536	2014, IKI-3106: Radiovalidation of the Extraction Efficiency of the Residue Analytical Method for Animal Tissues, DACO: 7.2.2,7.2.3B
2502019	2013, Acute Immobilisation Test of IKI-3106 50SL with *Daphnia magna,* DACO: 9.3.2
2524490	2015, IKI-3106 50 SL (80 g a.i. Cyclaniliprole / hectare): A semi-field study to evaluate potential effects on honeybee, *Apis mellifera* L. (Hymenoptera: Apidae), worker mortality and brood development following the application on *Phacelia tanacetifolia*, DACO: 9.2.8,IIIA 10.4.7
2612298	2014, Chronic Oral Toxicity Test of IKI-3106 50 SL on the Honey Bee (Apis mellifera L.) in the Laboratory, DACO: 9.2.4
2612300	2015, *Apis mellifera* larval toxicity test of IKI-3106, single oral exposure, DACO: 9.2.4
2614337	2016, Evaluation of Honeybee Colony Health and Productivity During and After Colony Exposure to Flowering Canola Fields Treated with IKI-3106 50 SL (Cyclaniliprole), DACO: 9.2.4
2663361	2016, Amended Report - IKI-3106 50SL: A Foliage Residue Toxicity Study with the Honeybee, DACO: 9.2.4
2667690	2016, IKI-3106: Translocation Study in Tomato, DACO: 8.5
2718601	2016, IKI -3106 Technical Grade: Honey Bee (*Apis mellifera*) Larval Toxicity Test, Repeated Exposure, DACO: 9.2.4

4.0 Value

PMRA#	Reference
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2399104	2011, Control of Lepidoptera Insects on Tomato, DACO: 10.2.3.4,IIIA 6.1.3.

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2399107	2011, Evaluate IKI-3106 of Control of Insects on Fruiting Vegetables, DACO: 10.2.3.4,IIIA 6.1.3.
2399108	2011, IKI-3106/Fruiting Vegetables/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399109	2011, IKI-3106 Pepper Insecticide, DACO: 10.2.3.4,IIIA 6.1.3.
2399110	2011, IKI-3106/Leaf Brassica Vegetables/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399111	2011, IKI-3106/Leaf Brassica Vegetables/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399112	2011, IKI-3106/Leaf Brassica Vegetables/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399113	2011, IKI-03106 Leafy Vegetables/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399114	2011, IKI-3106/Leafy Vegetables/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399115	2011, IKI-03106/Apples/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399116	2011, Efficacy of IKI-3106 For Control of Insects on Apples, DACO: 10.2.3.4,IIIA 6.1.3.
2399117	2011, IKI-3106/Stone Fruit/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399118	2011, IKI-3106/Almonds/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399119	2011, IKI-3106/Almonds/Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399120	2011, IKI-3106 Against Brassica Insect Pests in Cabbage, DACO: 10.2.3.4,IIIA 6.1.3.
2399121	2012, IKI-3106 Against Brassica Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399122	2012, IKI-3106 Against Cucurbit Insect Pests in Cucumbers, DACO: 10.2.3.4,IIIA 6.1.3.
2399123	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399124	2012, IKI-3106 Against Apple Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399125	2012, IKI-3106 Against Cherry Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399126	2012, IKI-3106 Against Brassica Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399127	2012, IKI-3106 Against Brassica Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399129	2012, IKI-3106 Against Brassica Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399130	2012, IKI-3106 Against Brassica Insect Pests (worms) on Broccoli, DACO: 10.2.3.4,IIIA 6.1.3.
2399133	2012, IKI-3106 Against Grape Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399134	2012, IKI-3106 Against Grape Insects, DACO: 10.2.3.4,IIIA 6.1.3.
2399135	2012, IKI-3106 Against Cucurbit Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399136	2012, IKI-3106 Against Cucurbit Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399138	2012, IKI-3106 Against Leafminer in Tomato, DACO: 10.2.3.4,IIIA 6.1.3.
2399139	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399140	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399141	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399142	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399143	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399144	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399145	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399146	2012, IKI-3106 Against Fruiting Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399147	2012, IKI-3106 Against Insect Pests – Lettuce, DACO: 10.2.3.4,IIIA 6.1.3.
2399148	2012, IKI-3106 Against Leafy Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399149	2012, IKI-3106 Against Leafy Vegetable Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399150	2012, IKI-3106 Against Apple Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399152	2012, IKI-3106 Against Apple Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399153	2012, IKI-3106 Against Apple Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399154	2012, IKI-3106 Against Cherry Insect Pests / OBLR, DACO: 10.2.3.4,IIIA 6.1.3.
2399155	2012, IKI-3106 Against Rhagoletis indefferens in Cherry / Western Cherry Fruit Fly, DACO: 10.2.3.4,IIIA 6.1.3.
2399156	2012, IKI-3106 Against Peach Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399157	2012, IKI-3106 Against Almond Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399158	2012, IKI-3106 Against Walnut Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399159	2013, IKI-3106 Against Cabbage Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399160	2013, IKI-3106 Against Brassica Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.

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2399161	2013, IKI-3106 Against Brassica Insect Pests in Cabbage with Simulated Aerial Application, DACO: 10.2.3.4,IIIA 6.1.3.
2399162	2013, IKI-3106 Against Brassica Insect Pests in Mustard Greens with Simulated Aerial Application, DACO: 10.2.3.4,IIIA 6.1.3.
2399163	2013, IKI-3106 Against Cucumber Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399164	2013, IKI-3106 Against Zucchini Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399165	2013, IKI-3106 Against Apple Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399166	2013, IKI-3106 Against Potato Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399167	2013, IKI-3106 Against Potato Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399168	2013, IKI-3106 Against Cherry Insect Pests Extension, DACO: 10.2.3.4,IIIA 6.1.3.
2399169	2013, IKI-3106 Against Peach Insect Pests Extension, DACO: 10.2.3.4,IIIA 6.1.3.
2399170	2013, Efficacy of IKI-3106 50g/L for Control of Lepidopteran Pests in Cabbage: Apex, North Carolina 2013, DACO: 10.2.3.4,IIIA 6.1.3.
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2399173	2013, IKI-3106 Against Peach Insect Pests Extension, DACO: 10.2.3.4,IIIA 6.1.3.
2399175	2013, IKI-3106 Against Almond Insect Pests, DACO: 10.2.3.4,IIIA 6.1.3.
2399176	2014, DACO 10.2.3.1 Efficacy Data Spreadsheet, DACO: 10.1 (OECD),10.2.3.4,IIIA 6.1.3.
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2532679	2015, 10.2.3.1 and 10.3.1 - Excel Spreadsheet - Cyclaniliprole SWD Efficacy Data, DACO: 10.1,10.2.3.1,10.3.1
2532680	2013, Management of Spotted Wing Drosophila in Cherry Orchards, 2013, DACO: 10.2.3.3
2532681	2013, Exp. 15-13: Fruit Fly Control in Tart Cherries, DACO: 10.2.3.3
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2532685	2014, Evaluation of Foliar Applications of IKI-3106 Against Lepidopteran Pests of Cranberries and Spotted Wing Drosophila (Blueberries), DACO: 10.2.3.3
2532686	2014, Efficacy of Insecticides on Drosophila suzukii (Matsumura) (Diptera: Drosophilidae), 2014, DACO: 10.2.3.3
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