Proposed Registration Decision PRD2026-02

Isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO

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Overview

Proposed Registration Decision for Isocycloseram

Health Canada's Pest Management Regulatory Agency (PMRA), pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Isocycloseram Technical, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO, containing the active ingredient isocycloseram. A21377 CP and A21708 CP are for the control of various insect and mite pests by foliar application on a broad range of field vegetables, fruit and nut trees, soybean, and peanut (and corn for A21708 CP). A22466 CP is for in-furrow application to control corn rootworms and wireworms in corn (field, seed and pop). EQUENTO RFC is a seed treatment product for the control of wireworms in dry lentils. A23294 TO, also containing the active ingredient chlorantraniliprole, is for the control or suppression of various pests in greenhouse ornamentals and turf.

Isocycloseram is currently registered for the control of cockroaches in commercial, industrial and residential buildings and other listed structures, and as a seed treatment product for the control of insect pests and for the control or suppression of seed-borne and soil-borne diseases on wheat, oat, barley, rye and triticale. For details, see Proposed Registration Decision PRD2025-11, *Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST*, and Registration Decision RD2026-03, *Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST*.

In the end-use product A23294 TO, isocycloseram is co-formulated with chlorantraniliprole. Chlorantraniliprole is currently registered to control a variety of insect pests in several agricultural crops, ornamentals and turf, to control subterranean termites in various sites, and as a seed treatment product on corn, cereals and dry legume vegetables to control or suppress various pests. For details, see Proposed Registration Decision PRD2016-08, *Chlorantraniliprole*, Registration Decision RD2016-17, *Chlorantraniliprole*, Proposed Registration Decision PRD2013-08, *Chlorantraniliprole*, Registration Decision RD2014-26, *Chlorantraniliprole*, Proposed Registration Decision PRD2010-27, *Chlorantraniliprole*, Registration Decision RD2011-02, *Chlorantraniliprole*, and ERC2008-03, *Chlorantraniliprole*.

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

This Overview describes the key points of the evaluation, while the Science evaluation provides detailed technical information on the human health, environmental and value assessments of isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO.

What does Health Canada consider when making a registration decision?

The primary objective of the *Pest Control Products Act* is to prevent unacceptable risks to individuals and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed

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

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

To reach its decisions, Health Canada's PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children). They also consider the unique characteristics of organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how Health Canada's PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and pest management portion of Canada.ca.

Before making a final registration decision on isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO, Health Canada's PMRA will consider any written comments received from the public directly related to the proposed decision in this consultation document.[3] Health Canada will then publish a Registration Decision[4] on isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

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

What is isocycloseram?

Isocycloseram is a new conventional chemical insecticide that targets the nervous system of insects and mites on contact and through ingestion. It is effective against agricultural pests when applied as a seed treatment, a foliar spray to plants or as an in-furrow treatment at planting.

Health considerations

Can approved uses of isocycloseram affect human health?

Products containing isocycloseram are unlikely to affect your health when used according to proposed label directions.

Potential exposure to isocycloseram may occur through the diet (food and drinking water), when handling and applying the end-use products, or when coming into contact with treated surfaces. When assessing health risks, two key factors are considered: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are selected 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

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

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

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

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 level at which no effects are observed. The health effects noted in animals occur at dose levels 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.

In laboratory animals, the technical grade active ingredient, Isocycloseram Technical, was of low acute toxicity by the oral, dermal and inhalation routes of exposure. Isocycloseram was non-irritating to the eyes and skin but caused an allergic skin reaction. Consequently, the hazard statement "POTENTIAL SKIN SENSITIZER" is required on the label.

The end-use product, A21377 CP, containing isocycloseram, was of low acute toxicity by the oral, dermal and inhalation routes of exposure. It was non-irritating to the eyes and skin and did not cause an allergic skin reaction.

The end-use product, A21708 CP, containing isocycloseram, was of low acute toxicity by the oral and inhalation routes of exposure. It was also classified as being of low acute toxicity by the dermal route of exposure. It was non-irritating to the skin, but was mildly irritating to the eyes and caused an allergic skin reaction. Consequently, the signal word and hazard statements "CAUTION – EYE IRRITANT" and "POTENTIAL SKIN SENSITIZER" are required on the label.

The end-use product, A22466 CP, containing isocycloseram, was of low acute toxicity by the oral and inhalation routes of exposure. It was also classified as being of low acute toxicity by the dermal route of exposure. It was non-irritating to the skin, but was corrosive to the eyes and caused an allergic skin reaction. Consequently, the signal word and hazard statements "DANGER – CORROSIVE TO EYES" and "POTENTIAL SKIN SENSITIZER" are required on the label.

The end-use product, EQUENTO RFC, containing isocycloseram, was of low acute toxicity by the oral and inhalation routes of exposure. It was also classified as being of low acute toxicity by the dermal route of exposure. It was minimally irritating to the eyes and skin and did not cause an allergic skin reaction.

The end-use product, A23294 TO, containing isocycloseram and chlorantraniliprole, was of low acute toxicity by the oral and inhalation routes of exposure. It was also classified as being of low acute toxicity by the dermal route of exposure. It was minimally irritating to the eyes, non-irritating to the skin and did not cause an allergic skin reaction.

Prior to the initial registration of isocycloseram, registrant-supplied short- and long-term (lifetime) animal toxicity tests, as well as information from the published scientific literature, were assessed for the potential of isocycloseram to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other potential human health hazards. The most sensitive endpoints for risk assessment were effects on body weight, altered fetal development, and reduced survival of the young. There was no evidence to suggest that isocycloseram damaged genetic material. An increase in ovarian tumours in female mice and

testicular tumours in male rats could not clearly be attributed to treatment with isocycloseram. There was an indication that the young were more sensitive than the adult animal. The risk assessment protects against the effects noted above and other potential effects by ensuring that the level of exposure to humans is well below the lowest dose level at which these effects occurred in animal tests.

Occupational risks from handling A21377 CP, A21708 CP, A22466 CP, and A23294 TO

Occupational risks are not of health concern when A21377 CP, A21708 CP, A22466 CP, and A23294 TO are used according to the proposed label directions, which include protective measures.

Workers mixing, loading or applying A21377 CP, A21708 CP, A22466 CP, and A23294 TO, and workers entering treated fields and greenhouses can be exposed to isocycloseram residues through direct skin contact or through inhalation. For A21377 CP, A21708 CP, A22466 CP and A23294 TO, the label specifies that workers must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during mixing, loading, application, clean-up and repair. In addition, for handheld application of A21377 CP, A21708 CP and A23294 TO, workers should wear eye, head and respiratory protection when applying above waist height, including overhead. For A21708 CP, the label also requires that workers wear protective eyewear (goggles or face shield) during open-cab airblast application. For A22466 CP, workers must also wear protective eyewear (goggles or face shield) during mixing, loading, clean-up and repair.

For A21377 CP, A21708 CP, and A22466 CP, the label requires that workers not enter or be allowed entry into treated fields during the restricted-entry interval (REI) of 12 hours. For A23294 TO, the label requires that workers not enter or be allowed entry into treated golf courses until sprays have dried. For sod farms and ornamentals grown in greenhouses, workers must not enter or be allowed entry during the REI of 12 hours.

Taking into consideration the label statements, the number of applications and the duration of exposure for handlers and postapplication workers, the risks to these individuals from exposure to A21377 CP, A21708 CP, A22466 CP, and A23294 TO are not of health concern when the end-use products are used according to the proposed label directions.

Occupational risks from handling EQUENTO RFC

Occupational risks are not of health concern when EQUENTO RFC is used according to the proposed label directions, which include protective measures.

Workers in commercial facilities (and mobile treaters) mixing, loading, calibrating equipment and treating lentil seeds, and those involved in bagging, sewing and stacking bags of treated seed, cleaning and repair and driving a forklift, can come in direct contact with isocycloseram residues on the skin and through inhalation. Therefore, these workers must wear the personal protective equipment and comply with the engineering controls specified in Appendix I, Table 1.

Farmers treating and planting lentil seeds and farmers planting commercially treated lentil seeds may also come in direct contact with isocycloseram through direct skin contact or inhalation. Therefore, farmers must also wear the personal protective equipment and comply with the

engineering controls specified in Appendix I, Table 1. In addition, for good hygiene practice, it is recommended that workers wear a NIOSH-approved N95 filtering facepiece respirator (dust mask) that is properly fit tested during all activities.

Taking into consideration the label statements and the durations of exposure for all workers, the risks to these individuals from exposure to EQUENTO RFC are not of health concern when the end-use product is used according to the proposed label directions.

Health risks in residential and other non-occupational environments

Risks in residential and other non-occupational environments are not of health concern when A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC, and A23294 TO are used according to the proposed label directions and REIs are observed.

A21377 CP and A21708 CP

A21377 CP and A21708 CP are not domestic class products; therefore, residential applicator risk assessments were not required. However, these end-use products are permitted for use on orchard crops (pome fruits, stone fruits, and tree nuts) which may be grown in residential areas. Adults and children can come into direct contact with isocycloseram when orchard trees on pick-your-own farms or residential properties are treated with A21377 CP and A21708 CP. Taking into consideration the label statements, the number of applications and the duration of exposure, the risks to individuals contacting treated trees are not of health concern when the end-use products are used according to the label directions.

A22466 CP and EQUENTO RFC

A22466 CP and EQUENTO RFC are not domestic class products, nor is residential exposure expected. Therefore, risks in residential and other non-occupational environments are not of health concern when used according to the proposed label directions.

A23294 TO

A23294 TO is not a domestic class product; however, it is proposed for use on turf in residential areas and on golf courses. Adults, youths and children golfing, and adults and youth participating in high contact activities on treated turf can come into direct contact with isocycloseram residues. Therefore, the label requires that individuals do not enter treated golf courses until sprays have dried. In addition, the label requires that for residential areas, individuals should not enter or be allowed to enter treated areas until sprays have dried. Taking into consideration the label statements, the number of applications and the duration of exposure, the risks to individuals golfing and contacting treated turf are not of health concern when used according to the proposed label directions.

Health risks to bystanders

Bystander risks are not of health concern when A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC, and A23294 TO are used according to the proposed label directions and spray drift restrictions are observed.

Standard label statements to protect against drift during application are on the labels. Therefore, health risks to bystanders are not of concern when the end-use products are used according to the proposed label directions.

Residue in food and drinking water

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

Aggregate acute dietary (food plus drinking water) intake estimates did not exceed 65% of the acute reference dose (ARfD) when head lettuce was removed from the dietary risk assessments for all population subgroups, including females 13–49 years. Initial aggregate acute dietary (food plus drinking water) intake estimates indicated that females 13–49 years are exposed to 115% of the acute reference dose (ARfD), and therefore are of health concern. As the risks are driven by the dietary contribution of head lettuce, the use of isocycloseram on head lettuce is not supported.

Aggregate chronic dietary (food (except head lettuce) plus drinking water) intake estimates indicated that the general population and all population subgroups are exposed to less than 22% of the acceptable daily intake, and therefore are not of health concern.

On the strength of the overall information, it was determined that a threshold approach was appropriate for the cancer risk assessment based on the observed tumours. Overall, the endpoints selected for the chronic dietary risk assessment are considered protective of the findings, including potential cancer effects.

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.* Given that dietary risks from the consumption of foods are shown to be acceptable when isocycloseram is used according to the supported label directions, which excludes head lettuce, MRLs are being proposed as a result of this assessment (refer to PMRL2026-03, *Isocycloseram*).

MRLs for isocycloseram determined from the acceptable residue trials conducted throughout Canada and the United States, including growing regions representative of Canada, in or on potatoes, leaf lettuce, spinach, mustard greens, cabbage, broccoli, cauliflower, tomatoes, bell peppers, non-bell peppers, eggplants, cucumbers, melons, squash, apples, pears, peaches, plums, cherries, almonds, pecans, field corn, popcorn, peanuts, dry beans, dry peas and dry soybeans can be found in the Science evaluation of this document.

Aggregate health risks from dietary and residential exposures

Aggregate risks to adults, youth and children from dermal contact to and consumption of isocycloseram residues are not of health concern when A21377 CP, A21708 CP, and A23294 TO are used according to the proposed label directions.

A21377 CP, A21708 CP, and A23294 TO

Adults and children can come into direct contact with isocycloseram residues when orchard trees on residential properties are treated with A21377 CP and A21708 CP. For A23294 TO, adults, youth and children can come into direct contact with isocycloseram residues during golfing and high contact lawn activities. Chronic dietary exposure to isocycloseram from food and drinking water must also be considered in the determination of aggregate risks. In turn, the aggregate risks to adults and children from dermal and dietary exposure are not of health concern when the end-use products are used according to the label directions.

Environmental considerations

What happens when isocycloseram is introduced into the environment?

When isocycloseram is used according to the label directions, the risks to the environment are acceptable for use as a foliar spray, in-furrow application, seed treatment and use in greenhouses.

Isocycloseram enters the environment when it is applied as a foliar spray, an in-furrow application and as a seed treatment. Limited environmental exposure is expected when isocycloseram is used in greenhouses. Isocycloseram may remain in soil for long periods of time. Isocycloseram has limited ability to move downward in the soil. As it may remain in the soil for long periods of time, isocycloseram may reach groundwater. Isocycloseram has the potential to run off into aquatic habitats. In water, isocycloseram is expected to move to sediment, where it remains for short to long periods of time depending on the type of water/sediment system and environmental conditions. Isocycloseram is not expected to build-up in the tissues of plants or animals. However, when used in accordance with the label directions, including all the required risk mitigation measures, the use is acceptable as a foliar spray outdoors and in greenhouses, as an in-furrow application and as a seed treatment application.

Value considerations

What is the value of A21377 CP, A21708 CP and A23294 TO?

The foliar application products A21377 CP and A21708 CP provide a new mode of action for use against insect and mite pests on a broad range of agricultural food crops.

The foliar application product A23294 TO provides a new mode of action against various insect and mite pests on a broad range of greenhouse ornamental crops and turf.

A21377 CP and A21708 CP provide control of various economically important pests on a broad range of field vegetables, fruit and nut trees, corn, soybean and peanut. Isocycloseram is a new active ingredient with a new mode of action for use against various pests (Appendix I, Tables

41–44), which will help manage resistance to the registered alternative pest control products. For a few of the pests, there are no other pest control products registered.

A23294 TO provides control of various economically important pests in greenhouse ornamental crops and turf. A23294 TO contains both isocycloseram and chlorantraniliprole, with isocycloseram providing a new mode of action for use against various pests of greenhouse ornamental crops and turf.

What is the value of EQUENTO RFC?

The seed treatment product EQUENTO RFC provides a new mode of action for control of wireworms in dry lentils.

Wireworms can reduce lentil plant stands and under high pest pressure can cause large economic damage to dry lentil crops. EQUENTO RFC will provide a new mode of action (IRAC Group 30 insecticide) for control of wireworm in lentils.

What is the value of A22466 CP?

The soil-applied pesticide A22466 CP provides a new active ingredient for control of corn rootworms and wireworms in corn.

Corn rootworms and wireworms can reduce plant stand of corn crops and under high pest pressure can cause large economic loss to corn crops. As a new active ingredient, A22466 CP will aid in resistance management of these pests in corn.

Measures to minimize risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law.

The key risk-reduction measures being proposed on the labels of Isocycloseram Technical, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

A21377 CP and A21708 CP

To reduce a risk of concern identified during the review, the use of isocycloseram on head lettuce is not supported. This was based on the risks of concern identified for females 13–49 years of age, driven by the dietary contribution of head lettuce. A risk-based MRL of 0.01 ppm (analytical method limit of quantitation) is proposed.

A21377 CP, A21708 CP, A22466 CP, and A23294 TO

To reduce the potential exposure of workers to isocycloseram through direct skin contact or inhalation of sprays, workers mixing, loading and applying A21377 CP, A21708 CP, A22466 CP and A23294 TO, and performing cleaning and repair activities must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. In addition, for handheld application of A21377 CP, A21708 CP, and A23294 TO, workers must wear eye, head and respiratory protection when applying above waist height, including overhead. For A21708 CP, workers must also wear protective eyewear (goggles or face shield) during open-cab airblast application. For A22466 CP, workers must wear protective eyewear (goggles or face shield) during mixing, loading, clean-up and repair. For A23294 TO, workers must not apply more than one single application at 1.11 L of product/ha per crop cycle for cut flowers grown in greenhouses.

For A21377 CP, A21708 CP, and A22466 CP, workers must not enter or be allowed entry into treated fields during the restricted-entry interval (REI) of 12 hours. For A23294 TO, workers must not enter or be allowed entry into treated golf courses until sprays have dried. For sod farms and ornamentals grown in greenhouses, workers must not enter or be allowed entry during the REI of 12 hours. Risks to workers are not of health concern when A21377 CP, A21708 CP, A22466 CP, and A23294 TO are used according to the proposed label directions and REIs are observed. Furthermore, a standard label statement to protect against drift during application is required.

EQUENTO RFC

To reduce the potential exposure of workers to isocycloseram through direct skin contact or inhalation of sprays, workers in commercial facilities (and mobile treaters) mixing, loading, calibrating equipment and treating lentil seeds, and those involved in bagging, sewing and stacking bags of treated seed, cleaning and repair and driving a forklift, must wear the personal protective equipment and comply with the engineering controls specified in Appendix I, Table 1.

Farmers treating and planting lentil seeds and farmers planting commercially treated lentil seeds must also wear the personal protective equipment and comply with the engineering controls specified in Appendix I, Table 1. In addition, for good hygiene practice, it is recommended that workers wear a NIOSH-approved N95 filtering facepiece respirator (dust mask) that is properly fit tested during all activities.

Risks to workers are not of health concern when EQUENTO RFC is used according to the proposed label directions. Furthermore, a standard label statement to protect against drift during application is present on the label.

Environment

A21377 CP and A21708 CP

- Precautionary label statements indicating toxicity to beneficial arthropods, bees and aquatic organisms.
- Precautionary label statements to indicate leaching to groundwater is possible.
- Best management practice label statements to reduce runoff entering aquatic habitats.

- Mandatory construction and maintenance of a vegetative filter strip of at least 10 metres wide between the edge of the application area and adjacent, downhill aquatic habitats.
- Spray buffer zones for the protection of sensitive terrestrial and aquatic habitats.
- Statements indicating that the use of isocycloseram as a foliar spray is not compatible with integrated pest management programs that use beneficial arthropods.
- For crops that are moderately to highly attractive to bees, limiting application to evenings when bees are not actively foraging.

A22466 CP

- Precautionary label statements indicating toxicity to aquatic organisms.
- Precautionary label statements indicating toxicity to bees and also informing users that the product is not systemic and therefore minimal exposure or risk is expected.
- Precautionary label statements to indicate leaching to groundwater is possible.
- Best management practice label statements to reduce runoff entering aquatic habitats.
- Mandatory construction and maintenance of a vegetative filter strip of at least 10 metres wide between the edge of the application area and adjacent, downhill aquatic habitats.

A23294 TO

- Precautionary label statements indicating toxicity to aquatic organisms, bees and certain beneficial arthropods.
- Precautionary statements to indicate leaching to groundwater is possible.
- Best management practice label statements to reduce runoff entering aquatic habitats.
- Mandatory construction and maintenance of a vegetative filter strip of at least 10 metres wide between the edge of the application area and adjacent, downhill aquatic habitats.
- Spray buffer zones for the protection of sensitive terrestrial and aquatic habitats.
- Label statements indicating that the use of isocycloseram as a foliar spray on turf is not compatible with integrated pest management programs that use beneficial arthropods.
- Label statements for use on turf in lawns indicating that the product is toxic to bees and not to be applied if the treatment area contains plants or weeds that are blooming, and that if applications must be made to areas that contain plants or weeds that are blooming, restrict applications to the evening when most bees are not foraging.
- Label statements requiring applications be made in a way that does not allow the product to drift to blooming plants or weeds and to minimize spray drift to habitats close to the application site.
- For greenhouse uses: precautionary label statements indicating that applications of isocycloseram are to be avoided when bees and beneficial arthropods are in the treatment area.
- For greenhouse uses: label statement restricting the product to not be used on blooming greenhouse ornamentals if plants are to be moved outdoors while sprayed blooms remain on the plant.
- Label statements prohibiting releases, effluent or runoff from greenhouses.

EQUENTO RFC

- Precautionary label statements indicating toxicity to aquatic organisms, bees, birds and small wild mammals.
- Label statements indicating that any spilled or exposed seeds and dust must be incorporated into the soil or otherwise cleaned-up from the soil surface.
- Best management practice label statements to reduce runoff entering aquatic habitats.
- Best management practice label statements to minimize bee exposure to dust during planting of treated seed.
- Precautionary label statements to indicate leaching to groundwater is possible.

Next steps

Before making a final registration decision on isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO, Health Canada's PMRA will consider any written comments received from the public that are directly related to this proposed decision, such as comments directed to the Science evaluation, in response to this consultation document up to 30 days from the date of publication (by 28 February 2026) of this document. If more time is required to provide comments, a request for an extension of an additional 15 days can be made. Your request must be submitted in writing to the PMRA's Publications Section (pmra.publications-arla@hc-sc.gc.ca) within the 30-day consultation period. 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 PMRA Publications, through the Public Engagement Portal (Public Engagement Portal forms – Consultation Comment). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada's response to these comments.

Other information

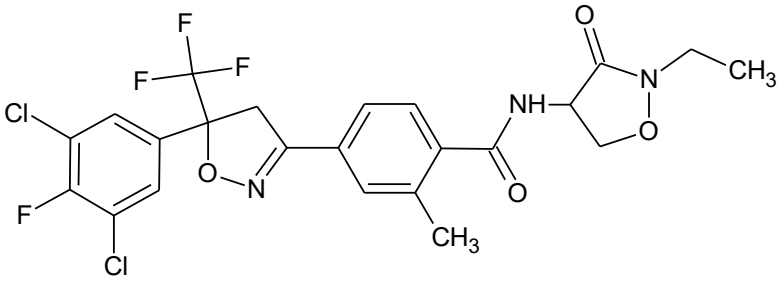
When Health Canada's PMRA makes its registration decision, it will publish a Registration Decision on isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO (based on the Science evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room. For more information or if you have questions, please contact the PMRA's Pest Management Information Service.

Science evaluation

Isocycloseram, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO

1.0 The active ingredient, its properties and uses

1.1 Identity of the active ingredient

Active substance	Isocycloseram
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Mixture comprised of 80–100% 4-[(5*S*)-5-(3,5-dichloro-4-fluorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl]-*N*-[(4*R*)-2-ethyl-3-oxoisoxazolidin-4-yl]-2-methylbenzamide and 20–0% of the (5*R*,4*R*), (5*R*,4*S*) and (5*S*,4*S*) isomers
2. Chemical Abstracts Service (CAS)	4-[5-(3,5-dichloro-4-fluorophenyl)-4,5-dihydro-5-(trifluoromethyl)-3-isoxazolyl]-*N*-(2-ethyl-3-oxo-4-isoxazolidinyl)-2-methylbenzamide
CAS number	2061933-85-3
Molecular formula	$C_{23}H_{19}Cl_2F_4N_3O_4$
Molecular weight	548.3
Structural formula	
Purity of the active ingredient	98 %

1.2 Physical and chemical properties of the active ingredient and end-use products

Technical Product— Isocycloseram Technical

Property	Result
Colour and physical state	white crystalline solid
Odour	sweetish
Melting range	135.3°C

Property	Result
Boiling point or range	not required for a solid
Density	1.53 g/cm^3 at 20°C
Vapour pressure	<6.2 × 10^{-6} Pa at 25°C
Ultraviolet (UV)-visible spectrum	1) Methanol (neutral solution) λ_{max} (nm) ε (L/(mol cm)) 265 2.50 × 10^4 2) Methanol (acidic solution) λ_{max} (nm) ε (L/(mol cm)) 265 2.26 × 10^4 3) Methanol (basic solution) λ_{max} (nm) ε (L/(mol cm)) 265 2.24 × 10^4 No absorption observed above 340 nm
Solubility in water at 20°C	1.2 mg/L
Solubility in organic solvents at 25°C	Solvent — Solubility (g/L) dichloromethane 400 acetone 270 ethyl acetate 190 methanol 75 toluene 33 n-hexane 39 n-octanol 17
n-Octanol-water partition coefficient (K_{ow})	log K_{ow} = 4.9 at 20°C
Dissociation constant (pK_a)	No dissociable protons in the pH range of 2–12
Stability (temperature, metal)	Stable when stored in contact with metals (Fe and Al) and metal salts (Fe(II) acetate and Al(III)acetate) at 40°C for 14 days

End-Use Product—A21377 CP

Property	Result
Colour	white
Odour	sweetish
Physical state	liquid
Formulation type	SU (suspension)
Label concentration	Isocycloseram 200 g/L
Container material and description	Plastic Jug (1 to 1000 L)
Density	1.07–1.11 g/mL at 20°C

Property	Result
pH of 1% dispersion in water	6.3
Oxidizing or reducing action	Not an oxidizing substance. Incompatible with strong oxidizers.
Storage stability	Stable in commercial packaging for 14 days at 54°C
Corrosion characteristics	Not corrosive to commercial packaging
Explodability	Not an explosive substance

End-Use Product—A21708 CP

Property	Result
Colour	dark brown
Odour	amine-like
Physical state	liquid
Formulation type	EC (emulsifiable concentrate)
Label concentration	Isocycloseram 100 g/L
Container material and description	Plastic Jug (1 to 1000 L)
Density	1.079 g/cm^3 at 20°C
pH of 1% dispersion in water	4.42
Oxidizing or reducing action	Not an oxidizing substance. Incompatible with strong oxidizers.
Storage stability	Stable in commercial packaging for 14 days at 54°C
Corrosion characteristics	Not corrosive to commercial packaging
Explodability	Not an explosive substance

End-Use Product—A22466 CP

Property	Result
Colour	off-white
Odour	weak aromatic
Physical state	liquid
Formulation type	SU (suspension)
Label concentration	Isocycloseram 300 g/L
Container material and description	Plastic Jug (1 to 1000 L)
Density	1.146–1.186 g/cm^3 at 20°C
pH of 1% dispersion in water	6.5
Oxidizing or reducing action	Not an oxidizing substance. Incompatible with strong oxidizers.

Property	Result
Storage stability	Stable in commercial packaging for 14 days at 54°C
Corrosion characteristics	Not corrosive to commercial packaging
Explodability	Not an explosive substance

End-Use Product—EQUENTO RFC

Property	Result
Colour	white
Odour	aromatic
Physical state	liquid
Formulation type	SU (suspension)
Label concentration	Isocycloseram 400 g/L
Container material and description	Plastic Jug or Tote (1 to 1050 L)
Density	1.12–1.18 g/mL at 20°C
pH of 1% dispersion in water	7.2
Oxidizing or reducing action	Not an oxidizing substance. Incompatible with strong oxidizers.
Storage stability	Stable in commercial packaging for 14 days at 54°C
Corrosion characteristics	Not corrosive to commercial packaging
Explodability	Not an explosive substance

End-Use Product—A23294 TO

Property	Result
Colour	off white
Odour	weak soap-like odour
Physical state	liquid
Formulation type	SU (suspension)
Label concentration	Chlorantraniliprole 110 g/L Isocycloseram 90 g/L
Container material and description	Plastic jug (0.5 to 100 L)
Density	1.07–1.11 g/cm^3 at 20°C
pH of 1% dispersion in water	7.86
Oxidizing or reducing action	Not an oxidizing substance.
Storage stability	Stable in commercial packaging for 14 days at 54°C
Corrosion characteristics	Not corrosive to commercial packaging
Explodability	Not an explosive substance

1.3 Directions for use

Foliar products, A21377 CP, A21708 CP, and A23294 TO

A21377 CP is a suspension formulation and A21708 CP is an emulsifiable concentrate which contain 200 g/L and 100 g/L isocycloseram, respectively. Both products are for foliar application to crop plants using conventional ground application equipment. For the control of a variety of insect and mite pests, both products are applied to a broad range of field vegetables, fruit and nut trees, soybean and peanut, and A21708 CP is also applied to corn. Application rates range from 50 to 150 mL A21377 CP per hectare and 100 to 300 mL A21708 CP (10 to 30 g a.i. per hectare) in spray volumes of 100 to 4000 litres of water per hectare, depending on the crop-pest combination. There is a maximum of 2 applications per year at rates up to 20 g a.i./ha with a minimum reapplication interval of 7 days or a single application per year at 30 g a.i./ha.

A23294 TO is a suspension formulation premix of isocycloseram (90 g/L) and chlorantraniliprole (110 g/L). A23294 TO is applied as a foliar application to control various pests of greenhouse ornamental plants and turf. Application to greenhouse ornamentals and turf is by conventional foliar spray by ground only. Application rates on ornamental plants range from 50 to 114 mL A23294 TO per 100 litres of water (4.5 to 10.3 g isocycloseram + 5.5 to 12.5 g chlorantraniliprole per 100 litres), and on turf at 555 mL A23294 TO (50 g isocycloseram + 61 g chlorantraniliprole per hectare) per hectare, depending on the pest/crop combination. One application can be made to turf. Up to 4 applications, applied at a minimum of 7–14 days apart, depending on the pest, may be applied to greenhouse ornamentals. A maximum of 2.0 L product (400 g a.i.)/ha/crop cycle may be applied to greenhouse ornamentals.

Seed treatment product, EQUENTO RFC

EQUENTO RFC is a seed treatment applied to seed prior to planting with commercial or on-farm seed treatment equipment.

EQUENTO RFC is a suspension formulation seed treatment insecticide containing 400 g/L isocycloseram. EQUENTO RFC is applied as a seed treatment for control of wireworm in lentils at rates of 6.25 to 12.5 mL product (2.5 to 5.0 g a.i.) per 100 kg seed. For in-season stand establishment and wireworm mortality, it is recommended to use the low rate for light to moderate wireworm populations. For fields with a history of wireworms and under high wireworm infestations, it is recommended to use the high rate.

In-furrow product, A22466 CP

A22466 CP is a suspension formulation containing the active ingredient isocycloseram at a concentration of 300 g/L. A22466 CP is applied in-furrow at planting. A22466 CP provides control of corn rootworms and wireworms in corn (field, seed, pop) and is applied at rates of 1.84 to 3.78 mL product (0.55 to 1.13 g a.i.) per 100 m row.

1.4 Mode of action

Isocycloseram is an Insecticide Resistance Action Committee (IRAC) Mode of Action Group 30 insecticide and miticide that blocks inhibitory neurotransmission by binding to gamma-aminobutyric acid (GABA) receptors, resulting in lethal hyperexcitation in insects. Isocycloseram is effective on contact and through ingestion. It does not have systemic activity in plants.

2.0 Methods of analysis

2.1 Methods for analysis of the active ingredient

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

2.2 Methods for formulation analysis

The methods provided for the analysis of the active ingredients in the formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for residue analysis

High-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes. For details, see PRD2025-11, *Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST*.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

Isocycloseram, also identified as SYN547407, is an isoxazoline insecticide. The pesticidal mode of action (MOA) of isocycloseram involves modulation of the gamma-aminobutyric acid (GABA)-gated chloride channel by allosterically blocking the GABA-activated chloride channel, causing hyperexcitation and convulsions in insects.

A detailed review of the toxicology database for isocycloseram was conducted previously and is summarized in the Proposed Registration Decision PRD2025-11, *Isocycloseram, VANECTO COCKROACH GET BAIT, EQUENTO and A23128 ST*. An extensive toxicology database is available for the assessment of human health risks of isocycloseram and is considered adequate to characterize the potential health hazards associated with isocycloseram. Toxicology reference values for use in the human health risk assessment were established previously and are reported in Appendix I, Table 2.

The end-use product, A21377 CP, containing isocycloseram, was of low acute toxicity via the oral, dermal, and inhalation routes of exposure in rats. It was non-irritating to the eyes and skin of rabbits, and was negative for skin sensitization when tested in mice using the local lymph node assay (LLNA).

The end-use product, A21708 CP, containing isocycloseram, was of low acute toxicity via the oral and inhalation routes of exposure in rats. Although no longer a routine data requirement, a waiver was granted for the acute dermal toxicity study on the basis that the oral hazard category is predictive for dermal hazard (SPN2017-03); therefore, A21708 CP was considered to be of low acute toxicity by the dermal route of exposure. It was mildly irritating to the eyes and non-irritating to the skin of rabbits, and was positive for skin sensitization when tested in mice using the LLNA.

The end-use product, A22466 CP, containing isocycloseram, was of low acute toxicity via the oral and inhalation routes of exposure in rats. Although no longer a routine data requirement, a waiver was granted for the acute dermal toxicity study on the basis that the oral hazard category is predictive for dermal hazard (SPN2017-03); therefore, A22466 CP was considered to be of low acute toxicity by the dermal route of exposure. It was non-irritating to the skin of rabbits, was considered to be corrosive to the eye, and was positive for skin sensitization in mice when tested using the LLNA.

The end-use product, EQUENTO RFC, containing isocycloseram, was of low acute toxicity via the oral and inhalation routes of exposure in rats. Although no longer a routine data requirement, a waiver was granted for the acute dermal toxicity study on the basis that the oral hazard category is predictive for dermal hazard (SPN2017-03); therefore, EQUENTO RFC was considered to be of low acute toxicity by the dermal route of exposure. It was minimally irritating to the eyes and skin of rabbits and was negative for skin sensitization when tested in mice using the LLNA.

The end-use product, A23294 TO, containing isocycloseram and chlorantraniliprole, was of low acute toxicity via the oral and inhalation routes of exposure in rats. Although no longer a routine data requirement, a waiver was granted for the acute dermal toxicity study on the basis that the oral hazard category is predictive for dermal hazard (SPN2017-03); therefore, A23294 TO was considered to be of low acute toxicity by the dermal route of exposure. It was minimally irritating to the eyes and non-irritating to the skin of rabbits, and it was negative for skin sensitization when tested in mice using the LLNA.

The results of acute toxicity studies conducted with the end-use products are summarized in Appendix I, Table 3.

3.2 Toxicology reference values

3.2.1 Route and duration of exposure

A21377 CP and A21708 CP

For mixers, loaders and applicators, exposure is characterized as short-term to intermediate-term in duration and is predominantly by the dermal and inhalation routes. For postapplication workers, exposure is characterized as short- to intermediate-term in duration and is

predominantly by the dermal route. Residential postapplication exposure would occur primarily via the dermal route and for a short-term duration.

A22466 CP

For mixers, loaders and applicators, exposure is characterized as short-term in duration and is predominantly by the dermal and inhalation routes. Given that A22466 CP is applied at planting through soil application, exposure to treated foliage is not expected for postapplication workers.

EQUENTO RFC

For workers in commercial seed treatment facilities, mobile seed treaters, and on-farm workers treating, planting and handling treated seeds, exposure is characterized as short- to intermediate-term in duration and predominantly by the dermal and inhalation routes.

A23294 TO

Exposure to mixers, loaders and applicators is characterized as short- to intermediate-term in duration and predominantly by the dermal and inhalation routes. For postapplication workers, exposure is expected to be predominantly by the dermal route, for a short- to intermediate-term duration when contacting treated turf and long-term duration when contacting greenhouse ornamentals. For residential and non-occupational scenarios, contact with treated turf in residential settings or golf courses would primarily occur via the dermal route for adults, youth and children (6 to <11 years) and via the oral route for children (1 to <2 years; residential settings only), for a short- to intermediate-term duration.

Isocycloseram is non-volatile with a vapour pressure of $<6.2 \times 10^{-6}$ Pa at 25°C. This vapour pressure is below the North American Free Trade Agreement (NAFTA) criterion for a non-volatile product at 1×10^{-5} kPa for indoor uses and 1×10^{-4} kPa for outdoor uses at 20–30°C. Therefore, inhalation risk is not of health concern for any postapplication scenario.

3.3 Dermal absorption

See PRD2025-11, *Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST*.

3.4 Occupational and residential exposure assessment

3.4.1 Acute hazards of end-use products and mitigation measures

A21377 CP

The acute hazard assessment indicated that A21377 CP is of low toxicity by the oral, dermal and inhalation routes of exposure. It is non-irritating to the eyes and skin and does not cause an allergic skin reaction. Based on these acute hazards, no additional personal protective equipment (PPE) is required.

A21708 CP

The acute hazard assessment indicated that A21708 CP is of low toxicity by the oral and inhalation routes of exposure. It is mildly irritating to the eyes and non-irritating to the skin but may cause an allergic skin reaction. Based on these acute hazards, eye protection is required during open-cab airblast application.

A22466 CP

The acute hazard assessment indicated that A22466 CP is of low toxicity by the oral and inhalation routes of exposure. It is corrosive to the eyes, non-irritating to the skin and may cause an allergic skin reaction. Based on these acute hazards, eye protection is required for workers during mixing, loading, clean-up and repair.

EQUENTO RFC

The acute hazard assessment indicated that EQUENTO RFC is of low toxicity by the oral and inhalation routes of exposure. It is minimally irritating to the eyes and skin and does not cause an allergic skin reaction. Based on these acute hazards, no additional PPE is required.

A23294 TO

The acute hazard assessment indicated that A23294 TO is of low toxicity by the oral and inhalation routes of exposure. It is minimally irritating to the eyes, non-irritating to the skin and does not cause an allergic skin reaction. Based on these acute hazards, no additional PPE is required for workers during mixing, loading, application, clean-up and repair.

3.4.2 Occupational exposure and risk assessment

Mixer, loader and applicator exposure and risk assessment

A21377 CP, A21708 CP and A22466 CP

Individuals have potential for exposure to isocycloseram during mixing, loading, application, clean-up and repair. For A21377 CP and A21708 CP, dermal and inhalation exposure estimates were generated from the Agricultural Handlers Exposure Task Force (AHETF) database and the Pesticide Handlers Exposure Database (PHED, v1.1) for mixers, loaders and applicators applying to tuberous and corm vegetables, leafy vegetables, Brassica head and stem vegetables, fruiting vegetables, cucurbit vegetables, corn (field, seed, pop), pome fruits, stone fruits, tree nuts, soybeans and peanuts using groundboom or airblast equipment. In addition, for orchard crops, dermal and inhalation exposures occur when using various handheld equipment: backpack, mechanically pressurized handgun, and manually pressurized hand wand.

For A22466 CP, dermal and inhalation exposure estimates were generated from the Agricultural Handlers Exposure Task Force (AHETF) database, for mixers, loaders and applicators applying in-furrow to corn (field, seed, pop) using groundboom equipment.

The personal protective equipment in the risk assessments are based on handlers wearing single layer and chemical-resistant gloves, socks and shoes (Appendix I, Table 4a).

Dermal exposure was estimated by combining the unit exposure values with the amount of product handled per day and the dermal absorption value of 8% and 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight.

Exposure estimates were compared to the selected toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 1000. Dermal and inhalation MOEs were combined, since the dermal and inhalation reference value was derived from the same oral toxicity study. Calculated MOEs were greater than the target MOE of 1000 for all chemical handler scenarios and are therefore not of health concern (Appendix I, Table 4b).

EQUENTO RFC

Commercial seed treatment (including mobile treaters) exposure and risk assessment

Lentil seeds can be treated in commercial seed treatment facilities, including mobile treaters. Individuals have the potential for exposure while treating lentil seeds using open or closed transfer equipment. Individuals also have potential for exposure while bagging, sewing and stacking bags of treated seed, during cleaning and repair of equipment and driving a forklift. Exposure estimates were generated using unit exposure values from scenario-specific surrogate passive dosimetry studies (owned by the Agricultural Handlers Exposure Task Force (AHETF)), which are summarized in Appendix I, Table 4c. These studies were considered the most appropriate for calculating occupational exposures.

The default throughput of 98 000 kg seed/day for lentils, for commercial seed treatment (including mobile treaters), was used. Exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption value of 8% and inhalation absorption value of 100%. Exposures were normalized to mg/kg bw/day by using 80 kg adult body weight. Exposure estimates were compared to the selected toxicological reference value to obtain the margins of exposure (MOE). Dermal and inhalation MOEs were combined since the toxicological reference values for both dermal and inhalation routes were derived from the same oral toxicity study. Calculated MOEs were greater than the target MOE of 1000 for all scenarios and are, therefore, not of health concern (Appendix I, Table 4d).

On-farm seed treatment and planting exposure and risk assessment

Lentil seeds can be treated on-farm; therefore, farmers have the potential for exposure while treating and planting lentil seeds using open transfer equipment. Exposure estimates were generated using an on-farm seed treatment and planting surrogate passive dosimetry study owned by AHETF. This study was considered the most appropriate for calculating on-farm treatment and planting exposure (Appendix I, Table 4e).

The throughput of 6000 kg seed treated and planted/day for lentils, for on-farm treatment and planting, was used. Exposure was estimated by coupling the unit exposure values with the amount of product handled per day and the dermal absorption value of 8% and inhalation absorption value of 100%. Exposures were normalized to mg/kg bw/day by using 80 kg adult body weight. Exposure estimates were compared to the selected toxicological reference values to

obtain the margins of exposure (MOE). Dermal and inhalation MOEs were combined since the toxicological reference values for both dermal and inhalation routes were derived from the same oral toxicity study. Calculated MOEs were greater than the target MOE of 1000 for all scenarios and are therefore not of health concern (Appendix I, Table 4f).

A23294 TO

Individuals have potential for exposure to isocycloseram during mixing, loading, application, clean-up and repair. Dermal and inhalation exposure estimates were generated from the Agricultural Handlers Exposure Task Force (AHETF) database, the Outdoor Residential Exposure Task Force (ORETF) database, and the Pesticide Handlers Exposure Database (PHED, v1.1) for mixers, loaders and applicators applying A23294 TO to turf using groundboom equipment and handgun lawn sprayer, and to ornamentals grown in greenhouses using various handheld equipment: backpack, mechanically pressurized handgun, and manually pressurized hand wand. The personal protective equipment in the risk assessment is based on handlers wearing single layer, chemical-resistant gloves, socks and shoes (Appendix I, Table 4g).

Dermal exposure was estimated by combining the unit exposure values with the amount of product handled per day and the dermal absorption value of 8% and inhalation absorption value of 100%. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight. Exposure estimates were compared to the selected toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 1000. Dermal and inhalation MOEs were combined, since the dermal and inhalation reference values were derived from the same oral toxicity study. Calculated MOEs were greater than the target MOE of 1000 for all chemical handler scenarios and are, therefore, not of health concern (Appendix I, Table 4h).

3.4.2.2 Postapplication occupational exposure and risk assessment

Chemical-specific data on apples, tomatoes, and turf were reviewed and relied on for assessing human exposures during postapplication activities.

3.4.2.2.1 Dislodgeable foliar residue (DFR) study – Apples

This study was designed to collect data to calculate dislodgeable foliar residue dissipation curves using apples grown at 3 test sites in the USEPA Regions 1, 5, and 10. The plots received three foliar airblast applications at a rate of 89–93 g a.i./ha per application on a 7 or 8-day retreatment interval (RTI). The application method and monitoring times were considered relevant to the proposed use patterns for the products A21377 CP and A21708 CP. The application rates and frequency of applications used in the study were higher than the supported rate and number of applications, in other words, a maximum of 2 applications of up to 0.02 kg a.i./ha or a single maximum application at 0.03 kg a.i./ha using ground application equipment only. The locations of the sites within the United States were considered geographically relevant to the Canadian growing and climatic regions, except the site in Region 10.

While there were uncertainties with the Region 1 site due to monthly rainfall, this site was selected as it was representative of Canada. As such, the % peak DFR after the second application of 22.4% was considered appropriate and selected for use in the risk assessment for apples and select orchard crops (stone fruits and tree nuts) with similar leaf texture (smooth/waxy), and updated use pattern: 2 applications of up to 0.02 kg a.i./ha at RTI = 7 days. For the supported use pattern of a single maximum application at 0.03 kg a.i./ha, the 10% peak DFR after the first application was considered appropriate. A daily dissipation of 1% was selected for both use patterns (Appendix I, Table 5a).

3.4.2.2.2 Dislodgeable foliar residue (DFR) study – Tomatoes

This study was designed to collect data to calculate dislodgeable foliar residue dissipation curves using tomatoes grown at 3 test sites in the USEPA Regions 1, 2, and 10. The plots received three foliar broadcast applications at a rate of 120–123 g a.i./ha per application on a 6 or 7-day retreatment interval. The application methods and monitoring times were considered relevant to the use pattern proposed. The application rates and frequency of applications used in the study were higher than the revised supported use pattern, in other words, a maximum of 2 applications of up to 0.02 kg a.i./ha, or maximum of 1 application at 0.03 kg a.i./ha permitted for ground application only. With the exception of Region 10, the locations of the trials within the United States are considered geographically relevant to the Canadian growing and climatic regions.

The Region 1 site had higher monthly rainfalls during the monitoring period when compared to the other sites which may have contributed to the high dissipation (15% per day) that was observed. It is expected that using the 15% dissipation rate might overestimate dissipation expected in Canada as the rainfall was greater than what is expected in Canadian growing regions. Given the 15% daily dissipation obtained for Region 1 (which had a lot of rainfall) and the 8% obtained for the Region 10 site (which is considered to be conservative of Canada as this site had no rain), it is expected that the daily dissipation will likely be around 10% which is consistent with the standard value. While the selection of the 10% dissipation rate for field crops is based on a weight-of-evidence, when combined with the peak values selected from the Region 1 site, it is not expected to underestimate residues for crops grown in Canada. As such, the % peak DFR after the second application of 41.7% was considered appropriate to model a 2 application use pattern at RTI = 7 days. For the supported use pattern of a single maximum application at 0.03 kg a.i./ha, the 20.13% peak DFR after the first application was considered appropriate (Appendix I, Table 5b).

3.4.2.2.3 Turf transferable residue (TTR) study

The study was designed to collect data to calculate turf transferrable residue (TTR) dissipation curves for isocycloseram at three trial sites in Regions 1, 2 and 10. Isocycloseram was applied twice at a rate of 147–151 g a.i./ha with 14 days between applications. The product was applied via tractor mounted boom or handheld boom sprayers. Transferable residues were sampled using the Modified California Roller Technique. Geographical and climatic conditions are comparable to various Canadian growing regions. The turf species at the Regions 1 and 10 sites (Kentucky bluegrass and Tall Fescue, respectively) are more commonly grown in Canada. At the Region 2 site, Bermudagrass was the tested species. While it is less commonly grown in Canada, it is grown in some regions. The turf grown at the Regions 1 and 10 sites are considered the most representative of the types of cool-season turf grown in Canada.

The study was considered acceptable for estimating turf transferrable residues of isocycloseram. The study had some minor limitations, none of which were considered to reduce the overall confidence in the study data. Considering the common types of turf grown in Canada (cool-season varieties) and the typical temperatures across several climatic zones in Canada, TTR data from the Region 1 site was recommended for use in the postapplication dermal exposure assessment as it addresses the residues observed at the other sites for the critical period shortly after application. Therefore, the peak TTR of 0.95% of the application rate after a single application and a dissipation rate of 20% per day from this site are recommended to model use patterns with different numbers of applications, different application rates and different retreatment intervals (Appendix I, Table 5c).

A21377 CP and A21708 CP

There is potential for exposure to workers entering areas treated with A21377 CP and A21708 CP to complete tasks such as scouting, hand weeding, hand harvesting, and handset irrigation. Given the nature of activities performed, exposure is primarily via dermal contact with treated foliage. Inhalation exposure is not expected as isocycloseram is considered non-volatile. As such, inhalation risk is not of health concern for postapplication workers as isocycloseram is considered to be non-volatile and the restricted-entry interval of 12 hours will allow residues to dry, suspended particles to settle and vapours to dissipate.

Dermal exposure to workers entering treated areas was estimated by coupling chemical-specific dislodgeable foliar residue (DFR) values with activity-specific transfer coefficients (TCs). Activity TCs are based on data from the Agricultural Re-entry Task Force (ARTF). Exposure estimates were compared to the toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 1000. Only exposures and risks to the activities with the highest TCs are presented as MOEs for these activities exceed the target MOE of 1000 and are, thus, not of health concern (Appendix I, Table 6a). For all postapplication activities, the REI of 12 hours is adequate.

A22466 CP

Given the proposed soil application (in-furrow at time of planting) to corn, exposure to postapplication workers is expected to be negligible.

EQUENTO RFC

Planter exposure and risk assessment

Commercially-treated seed are either bagged or stored in bulk. During planting, workers load the treated seed into a planter from bags or from bulk containers using an auger. Workers have the potential for exposure to EQUENTO RFC while loading and planting treated seed. Exposure estimates were generated using the maximum rate for lentils and unit exposure values from a planter surrogate passive dosimetry study owned by AHETF. This study was considered the most appropriate for calculating planter exposure (Appendix I, Table 6b).

The throughput used for planting commercially treated seeds was 6000 kg seed planted/day. Exposure was estimated by coupling the unit exposure values with the amount of product handled per day, the dermal absorption value of 8% and inhalation absorption value of 100%.

Exposures were normalized to mg/kg bw/day by using 80 kg adult body weight. Exposure estimates were compared to the selected toxicological reference values to obtain the margins of exposure (MOE). Dermal and inhalation MOEs were combined since the toxicological reference values for both dermal and inhalation routes were derived from the same oral toxicity study. The calculated combined MOE exceeded the target MOE of 1000 and is, thus, not of health concern (Appendix I, Table 6c).

A23294 TO

There is potential for exposure to workers entering areas treated with A23294 TO to complete tasks such as slab harvesting and transplanting/planting on sod farms; transplanting/planting, mowing, watering, cup changing, irrigation repair and miscellaneous grooming on golf courses and hand harvesting, scouting, hand weeding, transplanting, and ornamentals grown in greenhouses. Given the nature of activities performed, exposure is primarily via dermal contact with treated foliage and turf. Inhalation exposure is not expected as isocycloseram is considered non-volatile. As such, inhalation risk is not of health concern for postapplication workers as isocycloseram is considered to be non-volatile and the restricted-entry interval will allow residues to dry, suspended particles to settle and vapours to dissipate.

Dermal exposure to workers entering treated areas is estimated by coupling chemical-specific dislodgeable foliar residue (DFR) values and turf transferable residue (TTR) values with activity-specific transfer coefficients (TCs). Activity TCs are based on data from the Agricultural Re-entry Task Force (ARTF). Exposure estimates were compared to the toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 1000. Only exposures to the activities with the highest TCs are presented as MOEs for these activities exceed the target MOE of 1000 and are, thus, not of health concern (Appendix I, Table 6d). For sod farms, there are no health risks of concern and the REI of 12 hours is adequate to protect workers entering treated areas to conduct postapplication activities. For golf courses, health risks are not of concern for workers entering treated golf courses to conduct postapplication activities after the sprays have dried. For ornamentals grown in greenhouses (including cut flowers), no heath risks of concern were identified for workers conducting postapplication activities in greenhouses, except hand harvesting for cut flower production. The calculated MOE on the day of application exceeded the target MOE of 1000 only when the application rate to cut flowers was restricted to a single application of 0.1 kg a.i./ha/crop cycle (1.11 L/ha/crop cycle) (Appendix I, Table 6e).

3.4.3 Residential exposure and risk assessment

3.4.3.1 Handler exposure and risk assessment

A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC, and A23294 TO

A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC, and A23294 TO are not domestic class products, and are not permitted for use in residential settings; therefore, a residential handler exposure assessment is not required.

3.4.3.2 Postapplication residential exposure and risk assessment

A21377 CP and A21708 CP

A21377 CP and A21708 CP are permitted for use on pick-your-own (PYO) farms and on orchard crops (pome fruits, stone fruits, tree nuts) grown in residential areas. As such, a postapplication residential risk assessment is required.

A22466 CP and EQUENTO RFC

A22466 CP and EQUENTO RFC are not domestic class products and are not permitted for use in residential settings; therefore, a residential postapplication exposure assessment is not required.

A23294 TO

A23294 TO is proposed for use on turf which includes residential areas. As such, a postapplication residential risk assessment is required.

3.4.3.2.1 Pick-your-own (PYO) activities with A21377 CP and A21708 CP

Given that pome fruits, stone fruits, and tree nuts can be treated with isocycloseram, there is potential for exposure during pick-your-own activities. The postapplication occupational risk assessment is protective of the risk associated with dermal exposure to the patrons in a pick-your-own facility and, therefore, a quantitative risk assessment is not required.

3.4.3.2.2 Trees in residential areas treated with A21377 CP and A21708 CP

When a commercial applicator is hired to treat fruit and/or nut trees in a residential area or a farmer treats fruit and/or nut trees adjacent to residential areas, there is potential for residential postapplication dermal exposure to homeowners and their family.

The residential postapplication dermal risk assessment was conducted for adults (16+ years) and children (6 to < 11 years) when contacting treated fruit trees to perform activities such as hand harvesting, thinning, pruning, etc.

Dermal exposure was estimated using the chemical-specific DFR values of 22.4% deposition and 1% daily dissipation obtained from the apple DFR study, and the transfer coefficients, durations of exposure and body weights from the 2012 United States Environmental Protection Agency Residential Standard Operating Procedures. Using the dermal absorption value of 8% and toxicological reference values, calculated MOEs were greater the target MOE of 1000 (Appendix 1, Table 7a) for all residential postapplication exposure scenarios on Day 0. As such, health risks are not of concern and individuals can enter the treated area once the sprays have dried.

3.4.3.2.3 Golf courses treated with A23294 TO

There is the potential for postapplication exposure to isocycloseram for golfers (adults, youth and children) entering treated golf courses.

Dermal exposure to golfers is estimated by coupling the chemical-specific TTR of 0.95% of the application rate and 20% daily dissipation rate with the activity specific transfer coefficients, durations of exposure and body weights from the 2012 United States Environmental Protection Agency Residential Standard Operating Procedures. Using the dermal absorption value of 8% and the toxicological reference values, the calculated MOEs were all greater than the target MOE of 1000 (Appendix I, Table 7b). Therefore, health risks are not of concern for golfers entering treated golf courses after the sprays have dried.

3.4.3.2.4 Turf in residential areas treated with A23294 TO

There is the potential for postapplication dermal exposure to isocycloseram for adults (16+ years), youth (11 to < 16 years) and children (1 to < 2 years). Exposures to these individuals were estimated by coupling the chemical-specific TTR of 0.95% of the application rate and 20% daily dissipation rate with the activity specific transfer coefficients, durations of exposure and body weights from the 2012 United States Environmental Protection Agency Residential Standard Operating Procedures. Using the dermal absorption value of 8% and the toxicological reference values, the calculated MOEs were all greater than the target MOE of 1000 (Appendix I, Table 7c). Therefore, health risks are not of concern for individuals entering treated turf areas after the sprays have dried.

Children (1 to < 2 years) can also be exposed orally to isocycloseram from hand-to-mouth (HtM) and object-to-mouth (OtM) exposure. Using the dermal absorption value of 8% and the toxicological reference values, the calculated MOEs were all greater than the target MOE of 300 (Appendix I, Tables 7d and 7e). Therefore, health risks are not of concern for children playing on treated lawns after the sprays have dried.

3.4.4 Bystander exposure and risk assessment

Bystander exposure is considered negligible as application is limited when there is low risk of drift beyond the area to be treated, taking into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings.

Therefore, bystander exposure and risk are not of health concern since the potential for drift is expected to be minimal.

3.5 Dietary exposure and risk assessment

3.5.1 Exposure from residues in food of plant and animal origin

The residue definition for risk assessment and enforcement in plant commodities is isocycloseram. The data gathering and enforcement analytical methods are valid for the quantitation of isocycloseram residues in crop matrices. The residues of isocycloseram are stable in representative matrices from five commodity categories (high water, high oil, high protein, high starch, and high acid content) for up to 24 months, and up to 21 months in processed commodities when stored at ≤-18°C. The raw agricultural commodities (potatoes, field corn and peanuts) were processed, but were not further analyzed due to the lack of quantifiable residues when treated at exaggerated rates. Isocycloseram residues concentrated in the following processed commodities for human consumption: dried tomatoes (3.8×), dried prunes (3.2×), almond oil (5×) and roasted almonds (1.3×).

Crop field trials conducted throughout Canada (and the United States) using end-use products containing isocycloseram at exaggerated rates in or on potatoes, leaf lettuce, spinach, mustard greens, cabbage, broccoli, cauliflower, brussels sprouts, tomatoes, bell peppers, non-bell peppers, eggplants, cucumbers, melons, squash, apples, pears, peaches, plums, cherries, almonds, pecans, field corn, popcorn, peanuts, dry beans, dry peas, and dry soybeans are sufficient to support the proposed maximum residue limits. Field rotational crop studies were conducted in/on mustard greens, spinach, radish roots and wheat (forage, grain, hay, and straw). The data are adequate to demonstrate that a 120-day plant-back interval is appropriate for non-labeled crops.

3.5.2 Exposure from drinking water

For the human health risk assessment, estimated environmental concentrations (EECs) in potential drinking water sources are calculated for both groundwater and surface water using the Pesticide Water Calculator (PWC; version 2.001).

For surface water, the PWC calculates the amount of pesticide entering the water body by runoff and drift, and the subsequent degradation of the pesticide in the water system. EECs are calculated by modelling a total land area of 173 ha draining into a 5.3 ha reservoir with a depth of 2.7 m. Groundwater EECs are calculated by simulating leaching through a layered soil profile and reporting the average concentration in the 1 m below the water table.

Drinking water modelling follows a tiered approach consisting of progressive levels of refinement. Level 1 EECs are conservative values intended to screen out pesticides that are not expected to pose any concern related to drinking water. These are calculated using conservative inputs with respect to application rate, application method, application timing, and geographic scenario. Level 2 EECs are based on a narrower range of application timing, methods, and geographic scenarios, and are not considered conservative values that cover all regions of Canada. Only Level 1 modelling was required for isocycloseram.

For drinking water, the residue was defined as the combined residue of isocycloseram with fifteen of its transformation products (TPs): SYN549431, SYN549107, SYN551203, SYN550455, SYN549546, SYN551415, SYN550321, SYN550603, SYN549433, SYN550602, SYN551190, SYN549557, SYN548569, SYN549110 and SYN550737. Major transformation products (> 10% applied radioactivity (AR)) were included in the drinking water residue definition when it was determined that they are likely to form under environmental conditions. EECs for surface water were calculated based on a single standard scenario, which was simulated for 50 years. EECs in groundwater were calculated for several scenarios representing different regions of Canada; only the highest EECs from across these scenarios are reported. All groundwater scenarios were simulated for 100 years due to slow leaching. The major fate inputs used for the surface water and ground water modelling are presented in Tables 3.5.2.1 and 3.5.2.2, respectively. Level 1 EECs are reported in Table 3.5.2.3.

Table 3.5.2.1 Surface water model input parameters (transformation fractions in parenthesis)

Parameter	Parent[1]	Daughter1[2]	Daughter2[3]
Photolysis at 40° latitude (days)	240.80	Stable (0)	Stable (0)
Hydrolysis at pH 7 at 25°C (days)	347.10	Stable (0)	Stable (0)
Aerobic aquatic half-life at 21°C (days)	157.9	66.4[7] (1.0)	11.3 (0.839)
Anaerobic aquatic half-life at 20.9°C (days)	9.0	Stable (0.747)	624.7 (0.625)
Aerobic soil half-life at 20°C (days)	284.4	Stable (0)	Stable (0)
K_{oc} (L/kg)	1479.3	617.7	10

1 Parent as ICS + SYN551203 + SYN549431 + SYN549107 + SYN550737 + SYN549433 + SYN550602 + SYN550455 + SYN551190
2 Daughter1 as SYN548569 + SYN549546
3 Daughter2 as SYN550603 + SYN551415 + SYN550321 + SYN549557 + SYN549110

Table 3.5.2.2 Groundwater model input parameters

Parameter	Value
Hydrolysis half-life at pH 7 at 25°C (days)	347.10
Aerobic soil half-life at 20°C (days)	284.4
K_{oc} (L/kg)	1479.3

Table 3.5.2.3 Level 1 EECs of combined residues of isocycloseram and 15 of its TPs in potential sources of drinking water

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)		
	Peak[1]	Average[2]	Daily[3]	Yearly[4]	Overall[5]
1 × 44.8 g a.i./ha as seed treatment	0.065	0.055	1.3	0.21	0.18
1 × 150.3 + 2 × 29.7 g a.i./ha at 7-day as foliar applications	<0.30	<0.26	5.8	0.94	0.80
1 × 210 g a.i./ha as soil incorporation or in-furrow application	0.30	0.26	<5.8	<0.94	<0.80

1 The highest (peak) simulated average concentration in 1 m below the water table.
2 The temporal average concentration in the 1 m below the water table over the post-breakthrough simulation period.
3 90th percentile of the highest 1-day average concentration from each year.
4 90th percentile of yearly average concentrations.
5 Average of all yearly average concentrations.

3.5.3 Dietary risk assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 4.02, 05-10-c), which incorporates consumption data from the National Health and Nutrition Examination Survey/What We Eat in America (NHANES/WWEIA) for the year 2005-2010.

3.5.3.1 Acute dietary exposure results and characterization

The following refinements to the residue file inputs were applied to the basic acute exposure assessment: Canadian and/or American highest average field trial (HAFT) residues from field trials and experimental processing factors (where available). The refined acute dietary exposure for all proposed isocycloseram food uses was estimated to be 113% of the ARfD for females 13 to 49 years of age and 45–75% of the ARfD for all other subpopulations (95th percentile, deterministic).

A CCCA (Critical Contribution Commodity Analysis) was conducted indicating that head lettuce was the food that contributed the most to the risk for females 13–49 years of age.

When removing head lettuce from the exposure assessments, the refined acute dietary exposure for all remaining supported isocycloseram food uses was estimated to be 64% of the ARfD for females 13–49 years of age and 2–53% of the ARfD for all other subpopulations (95th percentile, deterministic). Aggregate exposure from food (except head lettuce) and drinking water (EEC value = 5.7 µg a.i./L, Level 1, surface water) is not of health concern. Specifically, 67% of the ARfD was obtained for females 13 to 49 years of age, and 2–56% for all other subpopulations.

3.5.3.2 Chronic dietary exposure results and characterization

The following refinements to the residue file inputs were applied to the basic chronic non-cancer exposure assessment: Canadian and/or American median residues from field trials and experimental processing factors for processed commodities (where available). The refined chronic dietary exposure from all supported isocycloseram food uses for the representative population subgroups ranged from 6% to 21% of the ADI. Aggregate exposure from food (except head lettuce) and drinking water (EEC value = 0.94 µg a.i./L, Level 1, surface water) is not of health concern. Specifically, a range from 6% to 22% of the ADI was obtained for all population subgroups. The highest exposed population subgroup was children 1 to 2 years of age.

3.6 Aggregate exposure and risk assessment

A21377 CP, A21708 CP, and A23294 TO

There is potential for individuals to be exposed to isocycloseram via different routes and sources of exposure concurrently. As such, the following scenarios were considered.

Aggregate chronic dietary (food and drinking water) and dermal exposures to isocycloseram from harvesting, pruning, thinning of trees in residential settings was conducted. When comparing the total (dietary and dermal) exposure to the aggregate toxicological reference

values, calculated MOEs were greater than the target MOEs (Appendix I, Table 8a) for all life stages. As such, aggregate health risks are not of concern.

For golfers and individuals contacting treated turf in residential areas, the chronic dietary exposures (food plus drinking water) were aggregated with the residential dermal exposures. Aggregate exposure estimates were compared to the aggregate toxicological reference values to obtain the MOE; the target MOE is 1000 for adults (16+ years) and youth (11 to <16 years), and 300 for children (6 to <11 years, and 1 to <2 years). The results of the aggregate risk assessment are presented in Appendix I, Tables 8b and 8c. The calculated MOEs were greater than the target MOEs and, as such, there are no health risks of concern.

3.7 Cumulative assessment

The *Pest Control Products Act* requires the PMRA to consider the cumulative effects of pest control products that have a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pesticides was undertaken for isocycloseram. Isocycloseram, along with broflanilide, cyproflanilide and fluxametamide, belong to a common pesticidal mode of action (MOA) group (Group 30) as determined by the Insecticide Resistance Action Committee (IRAC) that act as GABA-gated chloride channel allosteric modulators, inhibiting neurotransmission in insects. Treatment-related neurotoxic effects were not observed in the supporting isocycloseram database. This suggests that isocycloseram does not bind to vertebrate GABA receptors in the same capacity as it does to insect GABA receptors and that the pesticidal MOA in insects is not the same as the toxicological MOA in mammals.

Based on approved domestic and international uses for these pesticides, an assessment of a potential common mechanism of toxicity with fluxametamide and broflanilide was undertaken for isocycloseram. Cyproflanilide was not considered in this assessment as there are no registered uses in Canada or the US, and there are no American import tolerances or Codex MRLs.

Although the mammalian MOA for isocycloseram has not been elucidated, the available toxicity information demonstrated common toxicological effects between isocycloseram and other pesticides in the group. Specifically, isocycloseram and broflanilide both target the adrenal cortex, and isocycloseram and fluxametamide both target the small intestine (epithelial vacuolation) and affect sperm function. As such, it was determined that these three pesticides would form a common assessment group (CAG) for the purposes of a cumulative health assessment for repeated exposure scenarios (the common endpoints are not relevant to acute exposures).

For the purposes of this proposed registration of isocycloseram, a qualitative approach to assessing risks from cumulative exposure was undertaken for the pesticides within this CAG.

3.7.1 Isocycloseram and fluxametamide

Fluxametamide has a US tolerance for imported tea from Japan, resulting in the potential for exposure from imported foods. The USEPA concluded that risk from chronic exposure to fluxametamide from food only is less than 1% of the ADI for all population subgroups. As such, the contribution of fluxametamide to the cumulative risk with isocycloseram is minimal.

3.7.2 Isocycloseram and broflanilide

Table 3.7.2.1 presents the summary of uses and exposure pathways for isocycloseram and broflanilide.

Table 3.7.2.1 Summary of uses and exposure pathways for isocycloseram and broflanilide

Active ingredient	PMRA published document	Pesticide uses	Potential exposure pathways		
			Food	Drinking water	Residential
Broflanilide	PRD2020-06, RD2020-16	Foliar and soil application to potatoes, corn, sweet potato, CG 5-13, CG4-13, CG8-09, CSG22B and soybean, and seed treatment on small cereal grains	Yes	Yes (EEC[1])	No
Isocycloseram	Current assessment	Cockroach bait, seed treatment on small grain cereals and dry lentils, in-furrow treatment on corn, and foliar treatment on various crops, greenhouse ornamentals and turf	Yes	Yes (EEC[1])	No

[1] EEC = estimated environmental concentration; based on conservative modelling of pesticide residues in drinking water sources.

There is a potential for co-occurrence of exposure for the two pesticides. The contribution to the cumulative exposure of isocycloseram and broflanilide is expected through dietary (food and drinking water) exposure, as well as residential exposure from postapplication activities on treated golf course and residential turf. Only the scenario with the highest exposure (in other words, residential turf) was considered in the cumulative risk assessment as the other scenarios would contribute less and maximum postapplication exposures from both treated residential turf and golf courses are not expected to occur on the same day.

The most recent dietary risk assessment for broflanilide was conducted in 2023. No other expansion of use has been approved for broflanilide since then. The refined chronic dietary exposure from all supported food uses and imported foods for the representative population subgroups were less than 2% of the acceptable daily intake (ADI).

No acute reference dose was established for broflanilide. As such, a cumulative health risk assessment for acute exposure is not required.

When considering the estimated risks from the individual dietary exposure assessments (food and drinking water), chronic dietary exposure represented less than 22% of the ADI in the

refined chronic dietary exposure assessment for isocycloseram and less than 2% of the ADI in the refined chronic dietary exposure assessment for broflanilide. A simple sum of dietary exposure from the two active ingredients will be less than 24% of the risk cup for all subpopulations.

Taking into account the potential dermal and incidental oral postapplication exposure from treated residential turf, in addition to the chronic dietary exposure of isocycloseram, the aggregate exposure represented 28% and 36% of the risk cup for adults and children 1 to 2 years old, respectively. Summing these risk estimates with the chronic dietary risk of broflanilide for these subpopulations (1.3% and 1.9% of the ADI, respectively), it represents 30% and 38% of the risk cup, respectively.

The risk estimates from the individual pesticide assessments were calculated using the most conservative points of departure, that are not necessarily based on common effects on the adrenal cortex. As a result, the summing of these individual risk estimates overestimates the cumulative risk of isocycloseram and broflanilide.

Therefore, based on this qualitative assessment, the cumulative risks from potential co-exposure to GABA-gated chloride channel allosteric modulators through food and drinking water, where relevant, are acceptable.

3.8 Maximum residue limits (MRLs)

Dietary risks from the consumption of food commodities listed in Table 3.8.1 were shown to be acceptable for all population subgroups when isocycloseram is used according to the supported label directions. The approved label will not contain the originally proposed use on head lettuce because, when including it in the risk assessment, risks of concern were identified by the dietary contribution of head lettuce for females 13–49 years of age. All other foods containing residues at these levels are safe to eat. The PMRA recommends that the following MRLs be specified for residues of isocycloseram.

Table 3.8.1 Recommended maximum residue limits

MRL (ppm)	Food commodity
10	Leafy vegetables (crop group 4-13), except head lettuce
4.0	*Brassica* Head and Stem vegetable (crop group 5-13)
2.0	Dried tomatoes
1.5	Dried prune plums
1.0	Stone fruits (crop group 12-09)
0.6	Fruiting vegetables (crop group 8-09)
0.5	Almond oil
0.4	Pome fruits (crop group 11-09)
0.2	Tree nuts (crop group 14-11)
0.15	Cucurbit vegetables (crop group 9), dry soybeans
0.01	Head lettuce, tuberous and corm vegetables (crop subgroup 1C), field corn, dry lentils, peanuts, popcorn grain

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 section of Canada.ca.

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

For information on the nature of the residues in animal and plant matrices and analytical methodologies, see PRD2025-11. All other residue chemistry data, including field trial data, and acute and chronic dietary risk estimates are summarized in Appendix I, Tables 9 and 10.

3.9 Health incident reports

As of 28 August 2025, no human or domestic animal incidents involving isocycloseram have been submitted to Health Canada.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

Details on the fate and behaviour in the environment of isocycloseram can be found in PRD2025-11.

4.2 Environmental risk characterization

An environmental risk assessment was conducted as described in the guidance document Health Canada's Approach to Environmental Risk Assessment for Pest Control Products to estimate the potential for adverse effects on non-target species. Environmental exposure and ecotoxicology information were integrated by comparing EECs to effects-based values used to assess risk (effects metrics). EECs were estimated using standard models that consider application rates and chemical and environmental fate properties, including pesticide dissipation between applications. The EECs used in this risk assessment are presented in Appendix I, Tables 12, 13, 14 and 15.

Acute and chronic ecotoxicological data for non-target terrestrial, freshwater and marine organisms are summarized in Appendix I, Table 19. In the risk assessment, toxicity endpoints were adjusted via an uncertainty factor (UF) to calculate the effects metrics. The effects metrics account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population or individual level).

Initially, a screening-level risk assessment was performed using simple methods, conservative exposure scenarios and sensitive effects metrics. A risk quotient (RQ) was calculated by dividing the EEC by the effects metric and was then compared to the level of concern (LOC). When the screening level RQ was below the LOC, the risk was considered to be acceptable, and no further risk characterization was necessary. When the screening level RQ was equal to or greater than the LOC, a refined risk assessment was performed to further characterize the risk.

The refined risk assessment considered additional effects metrics as well as more realistic exposure scenarios, including runoff. Refinements to the risk assessment continued until the risk was adequately characterized or the available data did not permit further refinements.

Separate environmental risk assessments were conducted for outdoor foliar application, in-furrow application, seed treatment and indoor greenhouse uses as each of these use patterns result in different exposure scenarios.

4.2.1 Risk to non-target organisms from foliar application

4.2.1.1 Risk to terrestrial organisms from outdoor foliar application

When applied as a foliar spray, terrestrial organisms, such as earthworms and other soil-dwelling invertebrates, pollinators, birds and small wild mammals can be exposed to isocycloseram through direct contact of spray droplets during application, direct contact with sprayed surfaces, residues in soil or from ingestion of treated food sources, or soil or water containing residues. A risk assessment of isocycloseram and several of its transformation products was undertaken based on available toxicity data. Screening level EECs are presented in Appendix I, Tables 12, 13, 14 and 15. EECs for the major transformation products for which ecotoxicity data was available were calculated based on the EECs calculated for the parent and assuming that 100% of the parent transformed into each transformation product on a molar basis. See Appendix I, Table 11 for the molecular weight of each transformation product. Toxicity data is summarized in Appendix I, Tables 16 and 17. The screening level risk assessment for non-target terrestrial organisms (excluding birds and small wild mammals) for isocycloseram and its transformation products is presented in Appendix I, Table 20. The screening level risk assessment for birds and small wild mammals is presented in Appendix I, Table 27. Further risk characterization for non-target terrestrial organisms (excluding birds and small wild mammals) is presented in Appendix I, Tables 21, 22, 23, 24, and 25. Further risk characterization for small wild mammals is presented in Appendix I, Table 28.

The screening level RQs associated with the proposed use of isocycloseram as an outdoor foliar spray did not exceed the LOC for the following terrestrial organisms:

- Earthworms and other soil invertebrates
- Birds
- Terrestrial vascular plants

The screening level RQs associated with the proposed use of isocycloseram as an outdoor foliar spray did exceed the LOC for the following terrestrial organisms and further characterization of the risk was completed:

- Bees
- Beneficial arthropods
- Small wild mammals

Earthworms and other soil invertebrates

Earthworms and other soil invertebrates may be exposed to isocycloseram through residues in soil. Effects metrics for earthworms and collembola were compared to the screening level soil EEC. The resulting acute and chronic reproductive RQs did not exceed the LOC (RQ ≤ 0.2).

When used according to label directions, the risks to earthworms and other soil invertebrates from the use of isocycloseram as a foliar spray are acceptable.

Bees

Foraging bees could be exposed directly to isocycloseram via spray droplets during application, to residues on the surface of leaves (contact exposure), and through the ingestion of contaminated pollen and nectar (oral exposure). In addition, broods may be exposed to isocycloseram as foraging bees bring contaminated pollen and nectar back to the hive. The estimated contact and oral exposure for bees is compared to the effects metrics (expressed in µg a.i./bee) derived from laboratory toxicity studies. As such, the estimated exposure was converted from application rate (in kg a.i./ha) to an individual bee basis (in µg a.i./bee) using conversion factors as described in Appendix I, Table 12, for both the contact and oral bee assessments. Because individual flowers generally bloom for only a short period, it is unlikely that the same flower would receive more than one pesticide application. Accordingly, dietary exposure is estimated using a single maximum application rate rather than multiple cumulative applications.

For chronic adult and larval studies, the concentration-based endpoint (mg a.i./kg diet) was used in this risk assessment as it is considered more reliable than the daily-dose-based endpoint (µg a.i./bee/day). This is because it represents the exposure irrespective of bee growth and variations in daily food consumption throughout the study, which can be highly variable.

Isocycloseram has limited localized systemicity during early plant development. When applied as pre-bloom and post-bloom foliar applications, residues of isocycloseram are not anticipated to be taken up by plants and reach plant tissues such as pollen or nectar.

Screening level risk assessment

Effects metrics were compared to the screening level EECs. For adult bees, the LOC of 0.4, for acute exposure, was exceeded for contact and oral exposure (RQ: 0.5 and 5.1, respectively). The LOC of 1, for chronic dietary exposure, was also exceeded (RQ: 45). For larvae, the LOC of 0.4 for single dietary exposure and the LOC of 1 for repeated dietary exposure were also both exceeded (RQ: 1.3 and 49, respectively).

The LOC of 0.4, for adult bees exposed to the transformation product, SYN549106 (identified as SYN549431 in fate studies) was also exceeded for acute contact and acute oral exposure (RQ: 1.32 and 6.3, respectively). Risk towards bees was further characterized taking results from higher-tiered field studies into consideration.

RQs are only determined for honeybees, as the assumptions used in the calculations are based on honeybee data. As laboratory toxicity endpoints indicate that honeybees are more sensitive to isocycloseram than bumblebees, honeybees can be used as a surrogate for bumblebees.

Tier I refined

The screening level risk assessment is further refined by considering the toxicity endpoints from the laboratory toxicity studies and the measured residues from higher tier studies. Residues were available from semi-field studies where tunnels were set up to collect samples from either pollen, nectar, anthers, leaves, flowers, or from forager bees and/or pollen traps. Residues were considered for the parent only, as the transformation products, including SYN549106 (identified as SYN549431 in laboratory soil and aquatic fate studies), are not expected to be formed in the field since they were not found in pollen or nectar from plant residue studies. Out of these nine studies considered, residues from five studies were compared with the Tier I laboratory adult and larval effects metrics. Some studies represented residue collection from forager bees and pollen traps while others represented collection of pollen and nectar from plants. In all cases, application rates were higher than those proposed in Canada. Studies where residue data were not considered included those with heavy rainfall that potentially washed off residues underestimating exposure, and studies that were terminated early. Residues were available from studies with application to cotton, soybean, niger or phacelia, during bloom. For more details, see Appendix I, Tables 17 and 18.

The foliar application rates in the semi-field/residue studies were higher than the proposed foliar rate (1 × 50 g a.i./ha proposed for turf vs. cumulative rates between 82 and 149.9 g a.i./ha in the semi-field studies). The EECs and resulting RQs are thus conservative. To derive an acute EEC value for use in the refined acute oral risk assessment, the **maximum** foliar-applied residue values in pollen and nectar from each day from the residue studies were selected, when available. To derive a chronic EEC value for use in the refined chronic oral risk assessment, the **mean of the mean daily residue values** in pollen and nectar from all sampling days, when available, was selected from the semi-field studies with foliar applications during bloom. The mean of the mean field trial residue values was considered the most relevant for the chronic risk assessment as bees in the Tier I chronic studies are typically exposed to isocycloseram over a prolonged period of time (3 to 4 days for larvae and 10 days for adults) and gather pollen and nectar from multiple sources, rather than a single flower.

Based on residues in pollen and nectar, the acute adult RQs ranged from 0.04 to 0.83. The chronic adult RQs ranged from 0.11 to 1.3. The acute and chronic adult RQs only exceeded the LOC considering residues from one out of eight studies. For larva, all of the acute RQs were below the LOC of 0.4. Chronic larval RQs ranged from 0.28 to 1.5, and RQs exceeded the LOC considering residues from four out of eight studies. It is noted that all of the applications in the studies were higher than the proposed Canadian rates. Since the RQs were very close to both the acute and chronic LOC, it is expected that studies conducted with Canadian rates would result in lower residues, which would therefore not be expected to exceed the LOC. For more details, see Appendix I, Table 24.

Overall, considering the Tier I refined assessment, there was potential acute and chronic risk identified for adults and larva. However, this conclusion is based on RQ values very close to the LOC, and based on residues from application rates much higher than the proposed Canadian rate of 1 × 50 g a.i./ha. As such, this risk conclusion is considered very conservative. The results of the refined Tier I risk assessment will be considered in a weight of evidence approach in the overall conclusions for pollinators.

Tier II refined: Colony feeding study (CFS)

In a colony feeding study (CFS; PMRA No. 3246208), honey bees were fed technical grade isocycloseram at dietary concentrations of 0.078, 0.14, 0.20, and 0.28 mg a.i./kg diet in 50% sucrose solution for nine consecutive days followed by a 54-day monitoring period. Based on the data provided in the study, there did not appear to be any isocycloseram treatment-related effects on adult bees or brood up to the highest concentration tested of 0.28 mg a.i./kg diet. The NOEC based on mg a.i./kg diet was therefore determined to be 0.28 mg a.i./kg diet, which was compared to exposure estimates from measured pollen and nectar from semi-field studies as determined in the Tier I refined assessment. For more details, see Appendix I, Tables 17 and 18.

The highest mean-measured concentration in nectar (0.1377 ppm) from the semi-field studies was below the effects metric NOEC of 0.28 mg a.i./kg diet (equivalent to 0.28 ppm) from the sucrose CFS (Appendix I, Table 16). Colony feeding studies were only conducted with sucrose (and not pollen or pollen patties); as such, the nectar residues are the most direct exposure comparison to the NOEC. It is recognized that sucrose is a major source of food for bees, and consumption of nectar is much higher than pollen for adult bees. However, other castes of bees such as larva will consume residues in bee bread (which contains pollen) that would move through the hive from nectar. As a surrogate, the pollen residues were also compared to the NOEC (assuming the same effect to the colony from contaminated pollen as sucrose). The pollen residues range from 0.038 ppm (collected from cotton treated with 3 applications of 40 g a.i./ha during bloom) to 4.04 ppm (collected from forger bees following an application at 120 g a.i./ha to phacelia during bloom before hives were placed in tunnels). All of the applications were much higher than the proposed rate in Canada (1 × 50 g a.i./ha). As such, the residue levels in both nectar and pollen are expected to be much higher (and conservative for consideration in the risk assessment). Considering pollen residues collected from plants (0.038 ppm), the CFS NOEC of 0.28 ppm is much higher, indicating no exceedance of the effects metric (Appendix I, Table 25). When considering pollen residues from forager bees (range of 0.45 to 4.04 ppm), residues were higher than the CFS NOEC of 0.28 ppm, suggesting exceedance of the effects metric based on nectar consumption (Appendix I, Table 25).

It is important to note that there are added uncertainties with considering the pollen residues to the CFS since the dosing was done with sucrose and not pollen (or pollen patties). It is unknown if effects would be lower or higher from exposure to contaminated pollen patties. As such, endpoints from semi-field studies where pollen residues exceeded the CFS NOEC were assessed for effects. There were no lasting effects to brood development or colony strength in semi-field studies where pollen residues exceeded the CFS NOEC (PMRA No. 3246149 and 3246153). This would suggest there are negligible effects expected when comparing the CFS NOEC to residues. In addition, the NOEC from the study was the highest concentration tested, and the study did not observe any colony level effects.

Overall, considering the CFS effects metric compared to residues in pollen and nectar, including conservatisms and uncertainties, risk is not expected. The results of the refined Tier II risk assessment will be considered in a weight of evidence approach in the overall conclusions for pollinators.

Semi-field tunnel studies:

A total of nine semi-field tunnel studies were considered for further risk characterization towards bees. Five studies were conducted with isocycloseram being applied during active bee foraging and flight and four studies were conducted with isocycloseram applied either before or after active bee foraging and flight. Of the nine studies, two (PMRA No. 3246154 and 3246152) were not considered in the risk assessment owing to either heavy rainfall and lack of exposure, or early termination of the study because of poor control performance indicating issues with the overall study design. Summaries of the studies including test design, results, and overall conclusions are presented in Appendix I, Tables 17 and 18.

Considering all of the semi-field studies, when isocycloseram was applied during bloom during active bee foraging to an attractive crop (cotton) at rates higher than proposed Canadian rates, there were no effects to adults and limited effects to brood (only slight decline on day 7 in one study). When isocycloseram was applied during bloom without foraging bees (in other words, in the evening or before hives were placed in the field) to bee attractive crops (niger, buckwheat or phacelia) at rates higher than proposed Canadian rates, there were transient effects to brood and adults depending on the study and rate, with no overall colony level impacts. There is some uncertainty in the results since some studies with higher rates did not elicit effects (in other words, it was difficult to establish a rate dependent effect).

The risk assessment, including the colony feeding study and semi-field studies are expected to include exposure to any relevant transformation products that are formed in plants following application, including SYN549106 (identified as SYN549431 in fate studies), which was only formed at a maximum of 4.5% in field studies, but included in the screening level risk assessment for pollinators.

Overall conclusions for risk to bees:

Considering all of the information in a weight of evidence approach, there may be some effects to bees if applied during bloom when bees are actively foraging (without long term colony effects expected).

In order to reduce the risk towards bees, precautionary label statements to inform users of the toxicity of isocycloseram towards bees, as well as limiting the product to evening applications for crops that are moderately to highly attractive to bees, are required. The risks towards bees on crops that have low attraction towards bees are acceptable without limiting the product to evening applications. Crop by crop risk mitigation for bees is presented in Appendix I, Table 26.

When used according to label directions and in accordance with risk mitigation measures, the risks to bees from the use of isocycloseram as a foliar spray are acceptable.

Beneficial arthropods

Predatory and parasitic arthropods may be exposed to isocycloseram through spray droplets during application or to residues on plant and soil surfaces as well as direct contact with residues in the soil.

Effects metrics for the soil-dwelling predatory mite (*Hypoaspis aculeifer*) for isocycloseram were compared to the screening level soil EECs. The resulting RQs did not exceed the LOC (RQs: 0.02 to 0.1).

When used according to label directions, the risks to soil dwelling beneficial arthropods from the use of isocycloseram as a foliar spray are acceptable.

Additional laboratory toxicity studies were conducted on the soil-dwelling predatory mite, *Hypoaspis aculeifer*, exposed to the transformation products SYN547950, SYN549433 and SYN550918. Effects metrics were compared to the screening level soil EECs. The resulting RQs did not exceed the LOC (RQs: 0.0006 to 0.003).

When used according to label directions, the risks to soil dwelling beneficial arthropods from the transformation products of isocycloseram when isocycloseram is applied as a foliar spray are acceptable.

Effects metrics for exposure of the foliar dwelling predatory mite (*Typhlodromus pyri*) and the parasitic wasp (*Aphidius rhopalosiphi*) to isocycloseram were compared to the screening level foliar surface EECs. The resulting RQs exceeded the LOC for the predatory mite for both on-field (RQs: 5474 to 8475) and off-field (RQs: 508 to 4051) exposure scenarios as well as for the parasitic wasp for both on-field (RQs: 77 to 119) and off-field (RQs: 7 to 57) exposure scenarios.

Refined risk assessment for beneficial arthropods from exposure to isocycloseram

Refined EECs are presented in Appendix I, Table 12. The refined risk assessments for beneficial arthropods are presented in Appendix I, Tables 21 and 22.

Risk towards foliar dwelling beneficial arthropods were further characterized considering effects metrics from extended laboratory studies, foliar deposition fractions and dissipation between applications based on the field measured foliar DT_{50} of 4.7 days (90^{th} percentile based on 5 values). The foliar DT_{50} was also used to calculate the duration for which residues on foliage would be expected to exhibit a toxic effect (number of days the estimated residue concentrations exceed the effects metric before dissipating below the effects metric).

Effects metrics from the extended laboratory studies conducted with the predatory mite and parasitic wasp were compared to the refined EECs. The refined on-field and off-field RQs for the predatory mite for mortality and reproductive effects ranged from 2778 to 3617 and from 22 to 333, respectively. The refined on-field and off-field RQs for the parasitic wasp for mortality and reproductive effects ranged from < 8 to < 9 and < 0.07 to < 0.9, respectively.

For the predatory mite, the duration required for foliar residues to drop below the effects metric ranged from 55 to 108 days on-field and from 23 to 76 days off-field. For the parasitic wasp, the duration required for foliar residues to drop below the effects metric ranged from 14 to 26 days on-field, whereas off-field residual activity is not expected.

Based on the available information, isocycloseram is not considered compatible with certain beneficial arthropods in integrated pest management (IPM) programs. Parasitic wasps are known to control a variety of pests, including aphids, caterpillars, whitefly, mealybugs and scales, stink bugs and leaf miners. The specific pests they target may vary depending on the species of

parasitic wasp. In IPM, predatory mites are used to control various pests, with spider mites, thrips, and whiteflies being among the most common prey. While some species specialize on specific pests, others are polyphagous, meaning they can feed on a wider range of insects and mites. Although there may be some overlap in the function between predators and parasites (in other words, if one group declines in numbers, there may be other less susceptible groups that may increase in population owing to increased food availability), there also appears to be some unique pests for parasitic wasps that are different than predatory mites and, therefore, there may be some impacts for IPM depending on the target pest.

To mitigate the potential on-field exposure of beneficial arthropods to isocycloseram, all product labels with foliar applications must include precautionary statements indicating that isocycloseram is toxic to certain beneficial arthropods and advising users that isocycloseram is not compatible with IPM programs that use beneficial arthropods.

To mitigate the potential off-field exposure of beneficial arthropods to isocycloseram, terrestrial spray drift buffer zones are required on all product labels with outdoor foliar spay applications.

Birds and small wild mammals

Birds and small wild mammals may be exposed to isocycloseram through the ingestion of contaminated food sources. Effects metrics from the most sensitive species for birds and small wild mammals were compared to the screening level EDEs. For birds, the resulting RQs did not exceed the LOC for acute dietary risk (RQs: 0.1 to 0.3) nor for chronic reproductive risk (RQs: 0.1 to 0.3).

When used according to label directions, the risks to birds from the use of isocycloseram as a foliar spray are acceptable.

For small wild mammals, the resulting RQs did not exceed the LOC for acute oral risk (RQs: 0.005 to 0.01) nor for chronic reproductive risk for small-sized and large-sized small wild mammals (RQ: 0.7 for both). However, the LOC was slightly exceeded for reproductive risk for medium-sized small wild mammals (RQ: 1.3). Reproduction risk to medium-sized small wild mammals from isocycloseram was therefore further characterized.

The screening level risk assessment considered maximum on-field nomogram residues. When considering mean on-field residues, the LOC for reproductive risk was not exceeded for medium-sized small wild mammals (RQs: 0.0003 to 0.5).

When used according to label directions, the risks to small wild mammals from use of isocycloseram as a foliar spray are acceptable.

Terrestrial vascular plants

Terrestrial vascular plants may be exposed to isocycloseram directly via spray droplets during application or through residues on soil surfaces. Estimated Environmental Rates (EERs) for vegetative vigour were calculated based on the maximum proposed annual foliar application rate of 50 g a.i./ha, assuming direct overspray and accounting for foliar dissipation between applications. EERs for seedling emergence were calculated based on the maximum proposed

annual foliar application rate of 50 g a.i./ha, assuming direct overspray and accounting for soil degradation between applications.

Effects metrics were compared to the screening level EER of 50 g a.i./ha for vegetative vigour and seedling emergence, respectively. The resulting RQs did not exceed the LOC for vegetative vigour or seedling emergence (RQs: 0.1 and 0.1, respectively).

When used according to label directions, the risks to terrestrial plants from the use of isocycloseram as a foliar spray are acceptable.

4.2.1.2 Risk to aquatic organisms from foliar application

When isocycloseram is applied as a foliar spray, aquatic organisms, such as invertebrates, fish, amphibians, plants and algae, may be exposed to isocycloseram through spray drift and runoff entering aquatic habitats. A risk assessment for isocycloseram and several of its transformation products was undertaken based on available toxicity data. The toxicity data are summarized in Appendix I, Table 19.

Effects metrics of the most sensitive organism for each group of aquatic organisms were compared to the screening level EECs. Screening level aquatic EECs were converted from g a.i./ha to mg a.i./L based on the maximum proposed annual foliar application rate of 50 g a.i./ha, assuming 100% runoff from the application site into the water body and instantaneous complete mixing. Screening level aquatic EECs are presented in Appendix I, Table 14. EECs for major transformation products, for which toxicity data were available, were calculated based on the EECs of the parent and assuming that 100% of the parent transformed into each transformation product on a molar basis. See Appendix I, Table 11 for the molecular weight of each transformation product. The screening level aquatic organism risk assessment for isocycloseram and its transformation products is presented in Appendix I, Table 29. Further risk characterization for non-target aquatic organisms is presented in Appendix I, Tables 30, 31, 32, 33, 34 and 35.

The screening level RQs associated with the proposed use of isocycloseram as a foliar spray did not exceed the LOC for the following organisms:

- Freshwater and marine fish
- Freshwater vascular plants
- Freshwater and marine algae

The screening level RQs associated with the proposed use of isocycloseram as a foliar spray did exceed the LOC for the following aquatic organisms and further characterization of the risk was completed:

- Freshwater and marine invertebrates
- Amphibians

Aquatic invertebrates

Effects metrics from the most sensitive species were compared to the screening level EEC of 6.25 µg a.i./L for both freshwater and marine invertebrates. The resulting screening level RQs

exceeded the LOC for acute and chronic exposure scenarios for both freshwater invertebrates (RQs: 893 and 4808, respectively) and marine invertebrates (RQs: 694 and 1689, respectively). The risk to aquatic invertebrates from isocycloseram was, therefore, further characterized taking exposure from runoff and spray drift into consideration.

Additional studies conducted with the freshwater water flea (*Daphnia magna*) and the freshwater midge (*Chironomus riparius*) exposed to several transformation products of isocycloseram were available for this review. Effects metrics for the transformation products were compared to the screening level EECs of each corresponding transformation product. The resulting screening level RQs did not exceed the LOC for the water flea (RQs: 0.01 to 0.1). For the freshwater midge, the resulting screening level RQs did not exceed the LOC for SYN547950, SYN549433, SYN549546, SYN550455, SYN551113, SYN551513 or SYN551754 (RQs: 0.01 to 0.2). The screening level RQs did exceed the LOC for SYN550918 (identified as SYN550738 in the fate studies), SYN549431 and SYN551753 (identified as SYN550737 in the fate studies; RQs: 1.4 to 34).

The screening level RQs for these transformation products were greater than one order of magnitude lower than those of the parent. Mitigation put in place to mitigate risks to aquatic invertebrates from the parent will also be protective of any risk associated with the transformation products. The residue definition for modelling runoff EECs for the refined risk assessment was, therefore, limited to the parent only.

Refined aquatic risk assessment from exposure to isocycloseram

Refined EECs from runoff are presented in Appendix I, Table 12. The refined risk assessments for aquatic organisms from runoff and spray drift are presented in Appendix I, Tables 30, 31, 32, 33, 34 and 35.

Runoff:

The refined assessment considered modelled runoff EECs of various lengths of exposure compared to the closest matching effects metrics exposures for the most sensitive species of freshwater and marine invertebrates. Acute effects metrics based on 48- to 96-hour exposure scenarios were compared to the 24-hour and 96-hour modelled runoff EECs, respectively, and chronic effects metrics based on 21-day to 60-day exposures were compared to the 21-day and 60-day modelled runoff EECs, respectively. Runoff EECs from use on turf, orchard crops and non-orchard field crops were calculated individually as the modelled EECs from the different types of application equipment, different host crops and different application rates resulted in different exposure estimates.

For aquatic invertebrates, the refined acute and chronic RQs for the most sensitive species ranged from 1.1 to 48.

In order to mitigate the identified risk to aquatic invertebrates from runoff, standard label statements informing users of best management practices to reduce runoff into aquatic habitats are required in addition to the construction and maintenance of a vegetative filter strip of at least 10 metres wide between the edge of the application area and adjacent, downhill aquatic habitats.

When used according to label directions and in accordance with risk mitigation measures, the risk to aquatic invertebrates from runoff of isocycloseram and its transformation products are acceptable.

Spray drift:

The refined assessment considered modelled spray drift EECs 1 metre downwind based on an 80 cm water depth. Spray drift aquatic EECs from use on turf, orchard crops and non-orchard field crops were calculated individually as the modelled EECs from the different types of application equipment, different host crops and different application rates resulted in different exposure estimates. Aquatic EECs 1 metre downwind from spray drift are based on deposition factors of 6% for turf and non-orchard field crops (field sprayer equipment, medium droplet size) and 74% for orchard crops (airblast equipment, early season application).

A chronic freshwater study without sediment, where the test chemical is added to the water column, was not available for the most sensitive organism identified from the acute studies (*C. riparius,* a sediment-dwelling freshwater midge). Such a study was available for the freshwater water flea (*D. magna*). However, based on acute studies conducted on both the water flea and midge, the midge was shown to be significantly more sensitive than the water flea. In the absence of a chronic water column study conducted with *C. riparius*, the chronic 60-day effects metric from a sediment-spiked study with *C. dilutes* (expressed in µg a.i./L pore water) was compared to the modelled 60-day overlying water EEC instead of the typical modelled pore water EEC. This was done, as a conservative measure, to consider the possible chronic effects to pelagic freshwater invertebrates given that the modelled 60-day overlying water EECs are slightly higher than the 21-day modelled pore water EECs (Appendix I, Table 12). Although this may result in increased uncertainty in the chronic risk assessment towards pelagic freshwater invertebrates, this uncertainty is anticipated to be conservative in nature.

For aquatic invertebrates, the refined acute and chronic RQs for the most sensitive species ranged from 15 to 2812.

In order to mitigate the identified risk to aquatic invertebrates from spray drift, spray buffer zones are required.

When used according to label directions and in accordance with spray buffer zones, the risk to aquatic invertebrates from spray drift of isocycloseram and its transformation products are acceptable.

Fish and amphibians

Effects metrics of the most sensitive species were compared to the screening level EEC of 6.25 µg a.i./L for both freshwater and marine fish. The resulting RQs did not exceed the LOC for acute nor chronic freshwater and marine fish (RQs: < 1). However, the screening level RQ exceeded the LOC for amphibians (RQ: 2.8). The risk to amphibians from isocycloseram was, therefore, further characterized taking exposure from runoff and spray drift into consideration.

Refined aquatic risk assessment from exposure to isocycloseram

Refined EECs from runoff are presented in Appendix I, Table 12. The refined risk assessments for aquatic organisms from runoff and spray drift are presented in Appendix I, Tables 30, 31, 32, 33, 34 and 35.

Runoff:

For amphibians, the refined acute and chronic RQs for the most sensitive species ranged from 0.006 to 0.02.

When used according to label directions, the risk to fish and amphibians from runoff of isocycloseram and its transformation products are acceptable.

Spray drift:

For amphibians, the refined acute and chronic RQs for the most sensitive species ranged from 0.2 to 1.6.

In order to mitigate the identified risk to amphibians from spray drift, spray buffer zones are required.

When used according to label directions and in accordance with spray buffer zones, the risk to fish and amphibians from spray drift of isocycloseram and its transformation products are acceptable.

Vascular plants

Effects metrics were compared to the screening level EEC of 6.25 µg a.i./L. The resulting RQs did not exceed the LOC for freshwater aquatic plants (RQ: < 0.01). When used according to label directions, the risks to freshwater aquatic plants from the use of isocycloseram when used as a foliar spray are acceptable.

Algae

Effects metrics were compared to the screening level EEC of 6.25 µg a.i./L. The resulting RQs did not exceed the LOC for freshwater and marine algae (RQs: 0.02 to 0.03). When used according to label directions, the risks to freshwater and marine algae from the use of isocycloseram when used as a foliar spray are considered to be acceptable.

4.2.2 Risks to non-target organisms from in-furrow application

4.2.2.1 Risk to terrestrial organisms

When applied as an in-furrow application, terrestrial organisms, such as earthworms and other soil-dwelling invertebrates can be exposed to isocycloseram through direct contact within the soil. In-furrow applications are proposed for corn only and are to be applied only to the soil found within the furrow at the time of planting. Spray drift and residues on foliar surfaces from this application method are expected to be negligible. A risk assessment of isocycloseram and several of its transformation products was undertaken based on available toxicity data. Screening

level EECs from in-furrow application are presented in Appendix I, Table 14. EECs for the major transformation products for which ecotoxicity data were available, were calculated based on the EECs for the parent and assuming that 100% of the parent is transformed into each transformation product on a molar basis. See Appendix I, Table 11 for the molecular weight of each transformation product. Toxicity data is summarized in Appendix I, Table 16. The screening level risk assessment for terrestrial organisms from in-furrow is presented in Appendix I, Table 36.

The screening level RQs associated with the proposed use of isocycloseram as an in-furrow application did not exceed the LOC for the following terrestrial organisms:

- Earthworms and other soil invertebrates
- Bees
- Beneficial arthropods
- Birds
- Small wild mammals
- Terrestrial vascular plants

Terrestrial invertebrates

Earthworms and other soil invertebrates

Earthworms and other soil invertebrates may be exposed to isocycloseram through residues in soil. Effects metrics for earthworms and collembola were compared to the screening level soil EEC. The resulting acute and chronic reproductive RQs did not exceed the LOC (RQs $\leq$ 0.01).

When used according to label directions, the risks to earthworms and other soil invertebrates from the use of isocycloseram as an in-furrow application are acceptable.

Bees

In-furrow applications are proposed for corn only and are to be applied only to the soil found within the furrow at the time of planting. Spray drift and residues on foliar surfaces from this application method are expected to be negligible. As such, honey bees are not anticipated to be directly exposed through contact. Isocycloseram was determined to have limited localized systemicity during early plant development. Dietary exposure to bees by uptake of the chemical into growing plants from soil applications is therefore not anticipated.

When used according to label directions, the risks to bees from the use of isocycloseram as an in-furrow application are acceptable.

Beneficial arthropods

In-furrow applications are proposed for corn only and are to be applied only to the soil found within the furrow at the time of planting. Spray drift and residues on foliar surfaces from this application method are expected to be negligible. When used as an in-furrow application, exposure to non-target foliar-dwelling beneficial arthropods is not anticipated.

Soil-dwelling predatory mites may be exposed to isocycloseram through direct contact with residues in the soil. Effects metrics for the soil -dwelling predatory mite (*Hypoaspis aculeifer*) for isocycloseram and its transformation products were compared to the screening level soil EECs. The resulting RQs did not exceed the LOC (RQs: 0.2 to 0.7).

Additional laboratory toxicity studies were conducted on the soil predatory mite, *Hypoaspis aculeifer*, exposed to the transformation products SYN547950, SYN549433 and SYN550918. Effects metrics were compared to the soil EEC of 0.067 mg a.i./kg soil. The resulting RQs did not exceed the LOC for collembolans nor for soil-dwelling predatory mites (RQs: 0.002 to 0.004).

When used according to label directions, the risks to beneficial arthropods from the use of isocycloseram and its transformation products when applied as an in-furrow application are acceptable.

Birds and small wild mammals

Based on the proposed use pattern for in-furrow application where the product is sprayed directly in the furrow during seed planting, exposure to birds and small wild mammals from consumption of contaminated food sources or treated seeds is expected to be negligible.

When isocycloseram is used according to the directions for use, the risk to birds and small wild mammals from the use of isocycloseram as an in-furrow application are acceptable.

Terrestrial vascular plants

In-furrow applications are proposed for corn only and are to be applied only to the soil found within the furrow at the time of planting. Spray drift and residues on foliar surfaces from this application method are expected to be negligible. When used as an in-furrow application, exposure to non-target terrestrial vascular plants is not anticipated.

Based on a negligible exposure, when used according to label directions, the risks to terrestrial plants from the use of isocycloseram as an in-furrow application are acceptable.

4.2.2.2 Risk to aquatic organisms

When isocycloseram is applied as an in-furrow application, aquatic organisms, such as invertebrates, fish, amphibians, plants and algae, may be exposed to isocycloseram through runoff entering aquatic habitats. Exposure to aquatic organisms from spray drift is considered negligible for in-furrow applications, thus risks to aquatic organisms from spray drift of isocycloseram is considered acceptable. A risk assessment of isocycloseram and several of its transformation products was undertaken based on available toxicity data. The toxicity data are summarized in Appendix I, Table 19.

Effects metrics of the most sensitive organism for each group of aquatic organisms were compared to the screening level EECs. Screening level aquatic EECs were converted from g a.i./ha to mg a.i./L based on the maximum proposed annual application rate of 150 g a.i./ha, assuming 100% runoff from the treated furrows into the water body and instantaneous complete mixing. Screening level aquatic EECs are presented in Appendix I, Table 14. EECs for the major

transformation products for which ecotoxicity data were available were calculated based on the EECs of the parent and assuming that 100% of the parent transformed into each transformation product on a molar basis. See Appendix I, Table 11 for the molecular weight of each transformation product. The screening level aquatic organism risk assessment for isocycloseram and its transformation products is presented in Appendix I, Table 37. Further risk characterization for non-target aquatic organisms is presented in Appendix I, Table 37.

The screening level RQs associated with the proposed use of isocycloseram as an in-furrow application did not exceed the LOC for the following organisms:

- Freshwater vascular plants
- Freshwater and marine algae

The screening level RQs associated with the proposed use of isocycloseram as an in-furrow application did exceed the LOC for the following aquatic organisms and further characterization of the risk was completed:

- Freshwater and marine invertebrates
- Freshwater and marine fish
- Amphibians

Aquatic invertebrates

Effects metrics from the most sensitive species were compared to the screening level EEC of 18.75 µg a.i./L for both freshwater and marine invertebrates. The resulting screening level RQs exceeded the LOC for acute and chronic exposure scenarios for freshwater invertebrates (RQs: 2676 and 14423, respectively) as well as for marine invertebrates (RQs: 2083 and 5068, respectively). The risk to aquatic invertebrates from isocycloseram was therefore further characterized taking exposure from runoff into consideration.

Additional studies conducted with the freshwater water flea (*Daphnia magna*) and the freshwater midge (*Chironomus riparius*) exposed to several transformation products of isocycloseram were available for this review. Effects metrics for the transformation products were compared to the screening level EECs of each corresponding transformation product. The resulting screening level RQs did not exceed the LOC for the water flea (RQs: 0.02 to 0.4). For the freshwater midge, the resulting RQs did not exceed the LOC for SYN547950, SYN549433, SYN549546, SYN550455, SYN551113, SYN551513 or SYN551754 (RQs: 0.02 to 0.6). The screening level RQs did exceed the LOC for SYN550918 (identified as SYN550738 in the fate studies), SYN549431 and SYN551753 (identified as SYN550737 in the fate studies; RQs: 4.2 to 103).

The screening level RQs for these transformation products were greater than one order of magnitude lower than those of the parent. Mitigation measures put in place to mitigate risks associated with the parent will also serve to mitigate any risk associated with the transformation products. The residue definition for modelling runoff EECs for the refined risk assessment was, therefore, limited to the parent only.

Refined aquatic risk assessment from exposure to isocycloseram

Runoff:

Refined EECs from runoff are presented in Appendix I, Table 14. The refined risk assessments for aquatic organisms from runoff is presented in Appendix I, Table 38. The refined risk assessment for aquatic invertebrates from in-furrow application followed the same risk assessment framework used for foliar application (Section 4.2.1.2 Risk to aquatic organisms from foliar application).

For freshwater species, the refined acute and chronic RQs for the most sensitive invertebrate species were 24 and 32, respectively. For marine species, the refined acute and chronic RQs for the most sensitive invertebrates species were 16 and 19, respectively.

In order to mitigate the identified risk to aquatic invertebrates from runoff, standard label statements informing users of best management practices to reduce runoff into aquatic habitats are required in addition to the construction and maintenance of a vegetative filter strip of at least 10 metres wide between the application area edge and adjacent, downhill aquatic habitats. When used according to label directions and in accordance with risk mitigation measures, the risks to aquatic invertebrates from runoff of isocycloseram and its transformation products when used as an in-furrow application are acceptable.

Fish and amphibians

Effects metrics of the most sensitive species were compared to the screening level EEC of 18.75 µg a.i./L for both freshwater and marine fish. The resulting RQs exceeded the LOC for acute freshwater fish (RQ: 1.6) but did not exceed the LOC for chronic freshwater fish (RQ: 0.2). The screening level RQs for acute marine fish were not exceeded (RQ: 0.7) but they were exceeded for chronic marine fish (RQ: 2.4). For amphibians, the screening level RQs exceeded the LOC (RQ: 8.3). The acute risk to freshwater fish, chronic risk to marine fish and risk to amphibians were therefore further characterized taking exposure from runoff into consideration.

Runoff:

The refined acute RQ for the most sensitive freshwater fish species and the refined chronic RQ for the most sensitive marine fish species did not exceed the LOC (RQs: 0.01 and 0.01, respectively). The refined acute RQ for amphibians also did not exceed the LOC (RQ: 0.01).

When used according to label directions, the risk to freshwater fish, marine fish and amphibians from runoff of isocycloseram used as an in-furrow application on corn are acceptable.

Algae and aquatic plants

Effects metrics were compared to the screening level EEC of 18.75 µg a.i./L. The resulting RQs did not exceed the LOC for freshwater and marine algae nor for freshwater aquatic plants (RQs: < 0.03 to 0.09).

When used according to label directions, the risks to freshwater and marine algae and aquatic vascular plants from the use of isocycloseram used as an in-furrow application are acceptable.

4.2.3 Risks to non-target organisms from use in greenhouses

4.2.3.1 Risk to terrestrial organisms

When applied as a foliar spray in greenhouses, terrestrial organisms, such as pollinators and beneficial arthropods, can be exposed to isocycloseram through direct contact of spray droplets during application, direct contact with sprayed surfaces, residues in soil or from ingestion of treated food sources, or soil containing residues. A risk assessment of isocycloseram and several of its transformation products was undertaken based on available toxicity data. Earthworms, other soil invertebrates, birds, small wild mammals and terrestrial plants are not anticipated to be exposed to isocycloseram when it is applied as a foliar spray in greenhouses. Spray drift and residues on off-field foliar surfaces from this application method are also expected to be negligible. Screening level EECs are presented in Appendix I, Table 15. EECs for the major transformation products for which ecotoxicity data were available were calculated based on the EECs calculated for the parent and assuming that 100% of the parent transformed into each transformation product on a molar basis. See Appendix I, Table 11 for the molecular weight of each transformation product. Toxicity data are summarized in Appendix I, Table 16. The screening level risk assessment for pollinators and foliar-dwelling beneficial arthropods is presented in Appendix I, Table 39. Further risk characterization to pollinators and foliar-dwelling beneficial arthropods is presented in Appendix I, Table 40.

The screening level RQs associated with the proposed use of isocycloseram as a foliar spray in greenhouses exceeded the LOC for the following terrestrial organisms and further characterization of the risk was completed:

- Bees
- Beneficial arthropods

Earthworms, other soil invertebrates, birds, small wild mammals and terrestrial plants

When used as a foliar application in greenhouses, exposure to earthworms, other soil invertebrates, birds, small wild mammals and terrestrial plants is anticipated to be negligible.

When used according to label directions, the risks to earthworms, other soil invertebrates, birds, small wild mammals and terrestrial plants from the use of isocycloseram as a foliar spray in greenhouses are acceptable.

Bees

As bees may be used in greenhouse production for their pollination services, and sprayed ornamentals may be moved outside, the risks to bees from greenhouse applications of isocycloseram were determined. This risk assessment framework followed the same risk assessment framework used for outdoor foliar application (Section 4.2.1.2 Risk to aquatic organisms from foliar application). The assessment was conducted considering the proposed application rate for foliar spray in greenhouses of 150.3 g a.i./ha.

At the screening level, the LOC of 0.4 for acute exposure for adult bees was exceeded for contact and oral (RQ: 1.4 and 15.4, respectively). The LOC of 1 for repeat exposure/chronic dietary exposure was exceeded for adult bees (RQ: 134). The LOCs of 0.4 for single dietary exposure

and 1 for repeat exposure/chronic dietary exposure were also exceeded for bee larvae (RQ: 3.8 and 147, respectively).

The LOC of 0.4 for adult bees exposed to the transformation product, SYN549106 (identified as SYN549431 in fate studies) was also exceeded for acute contact and acute oral exposure (RQ: 4.0 and 19, respectively).

Risks towards bees from greenhouse applications was further characterized by considering the pollen and nectar residue data from the higher-tiered semi-field studies, as was done for the foliar uses (refer to Section 4.2.1.1 Risk to terrestrial organisms from outdoor foliar application). As stated in the foliar uses section, considering the residues and the effects metrics from the laboratory studies, there are LOC exceedances (Appendix I, Table 39). For outdoor foliar uses, these exceedances were considered to be conservative as the studies were conducted at rates much greater than the maximum outdoor foliar application rate of 50 g a.i./ha proposed for agricultural uses and turf. However, the proposed greenhouse application rates are much higher (150 g a.i./ha). As such, the application rates from the semi-field studies where effects were observed (rates up to 120 g a.i./ha) are considered more relevant to the proposed greenhouse rate.

The results of the tier II assessment comparing the colony feeding study (CFS) NOEC of 0.28 µg/kg to the pollen and nectar residues of semi-field studies determined some exceedances for pollen only (refer to Section 4.2.1.1 Risk to terrestrial organisms from outdoor foliar application). The limitations of considering pollen and the NOEC based on exposure to sucrose solution remain (as described in Section 4.2.1.1). However, unlike for outdoor foliar applications where the proposed rates were lower than those where residues were determined, the residues were determined from application rates similar (149.9 g a.i./ha) to (or even less than (60 g a.i./ha)) the proposed greenhouse foliar rates.

The results of the semi-field studies are discussed in the foliar uses section (Section 4.2.1.1 and in Appendix I, Tables 17 and 18). Overall, available studies conducted during bee foraging and during bloom (cumulative rates of 82 and 149.9 g a.i../ha, respectively) were at or below the proposed greenhouse rate of 150 g a.i./ha, and therefore provide some insight into potential effects from greenhouse applications. Considering semi-field studies conducted in the evening at rates more relevant for the greenhouse rate, there were some effects observed to either brood or adults. One of the studies on honey bees (PMRA No. 3246151) conducted at 149.9 g a.i./ha resulted in potential transient mortality to adults (and no apparent effects to brood); and another study (PMRA No. 3246153) conducted at 124.2 g a.i./ha resulted in effects to brood over multiple days (days 3, 7, 13 and 20), with no effects on adult mortality.

Consistent with the foliar use assessment, some potential risk was identified following a tier I, tier I refined, tier II refined and semi-field tunnel risk assessments. Due to the higher application rate in greenhouses, there is less uncertainty with the assessment than for outdoor foliar applications. As some residue and colony effects studies were done at rates more relevant to greenhouse rates, it was concluded that potential risks may exist if applications are made during bloom to pollinator attractive crops. As ornamentals are highly attractive to bees, precautionary label statements are required indicating risks to bees used in greenhouse production, and that applications of isocycloseram are to be avoided when bees are in the treatment area. Additionally, plants sprayed during bloom should not be moved outdoors while the sprayed blooms remain on the plant.

Beneficial arthropods

Predatory and parasitic arthropods may be exposed to isocycloseram through spray droplets during application or to residues on plant and soil surfaces.

Effects metrics for exposure of the foliar dwelling predatory mite (*Typhlodromus pyri*) and parasitic wasp (*Aphidius rhopalosiphi*) for isocycloseram were compared to the screening level foliar surface EECs. Spray drift from foliar spray in greenhouses is expected to be negligible. The risks to foliar dwelling beneficial arthropods from use of isocycloseram in greenhouses was therefore conducted considering on-field (in the greenhouse) exposure only. The resulting RQs exceeded the LOC for the predatory mite (RQ: 28574) as well as the parasitic wasp (RQ: 401). Risk towards foliar dwelling beneficial arthropods were further characterized considering effects metrics from extended laboratory studies, foliar deposition fractions and dissipation between applications based on the field measured foliar DT_{50} of 4.7 days (90^{th} percentile based on 5 values).

Effects metrics from the extended predatory mite and parasitic wasp studies were compared to the refined estimated exposures. The resulting refined RQs for the predatory mite exceeded the LOC for mortality and reproductive effects (RQs: 17875 and 21450, respectively). The RQs for the parasitic wasp also exceeded the LOC for mortality and reproductive effects (RQs: 52 and 53, respectively). Based on the refined RQs, isocycloseram is not considered compatible with certain beneficial arthropods in IPM programs.

To mitigate the potential on-field (inside the greenhouse) exposure of beneficial arthropods to isocycloseram, all product labels with foliar applications in greenhouses must include precautionary statements indicating that isocycloseram is toxic to certain beneficial arthropods and precautionary label statements indicating that applications of isocycloseram may harm certain beneficial arthropods used in greenhouse production and to avoid application when beneficial arthropods are in the treatment area. Off-field exposure of beneficial arthropods to isocycloseram from use in greenhouses is expected to be negligible.

When used according to label directions and in accordance with risk mitigation measures, the risks to beneficial arthropods when used as a foliar spray in greenhouses are acceptable.

4.2.3.2 Risk to aquatic organisms

Label statements prohibiting the releases of effluent or runoff from greenhouses containing this product to enter lakes, streams, ponds or other waters are required on the product label. Exposure to aquatic organisms through runoff or spray drift, from the use of isocycloseram as a foliar spray in greenhouses, is anticipated to be negligible.

When used according to label directions, the risks to aquatic organisms from the use of isocycloseram as a foliar spray in greenhouses are acceptable.

4.2.4 Risks to non-target organisms from seed treatment

The review of isocycloseram as a seed treatment was previously reviewed under PRD2025-11, *Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST*. The

proposed use pattern for seed treatment of lentil seeds at a maximum application rate of 5.0 g a.i./100 kg seed falls within the use pattern previously reviewed under PRD2025-11.

When used according to label directions, the risks to non-target organisms from the use of isocycloseram as a seed treatment on lentil seeds are acceptable.

4.2.5 Environmental review of co-formulated active ingredients

The proposed end-use product, A23294 TO, is a co-formulation of isocycloseram (90 g/L) and chlorantraniliprole (110 g/L).

The proposed rates for the co-formulated active ingredient fall within current registered use pattern. The environmental risk assessments for chlorantraniliprole (ERC2008-03, *Chlorantraniliprole*) may be consulted for additional information on this active ingredient.

4.2.6 Environmental incident reports

As of 28 August 2025, no environmental incident reports involving isocycloseram have been submitted to Health Canada.

5.0 Value

Foliar products

A21377 CP and A21708 CP provide a new mode of action for use against all of the supported pests. Most of the supported uses involve common and widespread pests and crops in Canada, for which there are numerous alternatives registered, including various modes of action. Isocycloseram provides a new mode of action that will help the management of resistance to active ingredients registered for most of the pests. For a few of the pests, there are no alternatives registered.

Numerous field trials, combined with rationales to extrapolate among crops, were sufficient to support use of A21377 CP and A21708 CP for control of various insect and mite pests on a wide range of terrestrial food crops, including a variety of vegetable crops, fruit and nut trees, corn, soybean and peanut.

The isocycloseram component of A23294 TO provides a new mode of action against all supported pests of greenhouse ornamentals and turf. Value information submitted in support of the proposed claims on turf included field trials on all supported turf pests. A rationale to extrapolate control from similar claims on ACELEPRYN Insecticide (Reg. No. 28980; chlorantraniliprole) was also submitted. Value information for greenhouse ornamental claims consisted of trials conducted on some of the pests and a rationale to extrapolate the remaining pest claims from similar claims on the ACELEPRYN Insecticide label. The submitted value information was sufficient to support a claim that A23294 TO provides control of various pests in greenhouse ornamentals and turf. Some of the ornamental pests claims were limited to specific ornamental crops where the pest was host-specific.

Seed treatment product

EQUENTO RFC provides a new mode of action (IRAC Group 30 insecticide) for control of wireworm in lentils. Value information submitted to support the claims for EQUENTO RFC consisted of field efficacy trials on wireworm in lentils. The value information was sufficient to support a claim that EQUENTO RFC provides control of wireworm in lentils.

In-furrow product

The soil-applied pesticide A22466 CP provides a new active ingredient for control of corn rootworms and wireworms in corn. Corn rootworms and wireworms can reduce plant stand of corn crops and under high pest pressure can cause large economic loss to corn crops. As a new active ingredient, A22466 CP will aid in resistance management of these pests in corn. Value information submitted to support the label claims for A22466 CP consisted of efficacy trials on western corn rootworm and wireworms. The submitted value information was sufficient to support a claim that A22466 CP will provide control of corn rootworms and wireworms in corn (field, seed, pop) in-furrow at planting.

Further details of the supported uses of each of the above products are listed in Appendix I, Tables 41–44.

6.0 Pest Control Product Policy considerations

6.1 Toxic Substances Management Policy considerations

Details on the Toxic Substances Management Policy (TSMP) assessment of isocycloseram are found in PRD2025-11, *Isocycloseram, VANECTO COCKROACH GEL BAIT, EQUENTO and A23128 ST*.

Health Canada has reached the conclusion that isocycloseram and its transformation products do not meet all of the TSMP Track 1 criteria.

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.* The list is used as described in the Science Policy Note SPN2020-01 and is based on existing policies and regulations, including the Toxic Substance Management Policy and Formulants Policy, and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives Regulations* under the *Canadian Environmental Protection Act, 1999*, (substances designated under the *Montreal Protocol*).

Health Canada has reached the conclusion that isocycloseram and its end-use products, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO do not contain any formulants or contaminants identified on Parts 1 or 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

7.0 Proposed regulatory decision

Health Canada's PMRA, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Isocycloseram Technical, A21377 CP, A21708 CP, A22466 CP, EQUENTO RFC and A23294 TO. A21377 CP, containing isocycloseram, is for the control of various insect and mite pests by foliar application on a broad range of field vegetables, fruit and nut trees, soybean, and peanut. A21708 CP, containing isocycloseram, is for the control of various insect and mite pests by foliar application on a broad range of field vegetables, fruit and nut trees, corn, soybean, and peanut. A22466 CP, containing isocycloseram, is for in-furrow application to control corn rootworms and wireworms in corn (field, seed and pop). EQUENTO RFC, containing isocycloseram, is a seed treatment product for the control of wireworms in dry lentils. A23294 TO, containing isocycloseram and chlorantraniliprole, is for the control or suppression of various pests in greenhouse ornamentals and turf.

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

List of abbreviations

↑	increased
↓	decreased
♀	female
♂	male
>	greater than
<	less than
λ	wavelength
µg	microgram(s)
°C	degrees Celsius
a.i.	active ingredient
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
ATPD	area treated per day
atm	atmosphere
BBCH	Biologishe Bundesanstalt, Bundessortenamt and Chemical industry
BP	backpack
bw	body weight
bwg	body weight gain
CAF	composite assessment factor
CAG	common assessment group
CAS	Chemical Abstracts Service
CCCA	Critical Contribution Commodity Analysis
CEPA	Canadian Environmental Protection Act
CFS	colony feeding study
cm	centimetres
cm^3	cubic centimetre(s)
CR	chemical-resistant
d	day(s)
DAA	days after application
DBA	days before application
DACO	data code
DAE	days after exposure
DAT	days after treatment
DFR	dislodgeable foliar residue
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
dw	dry weight
EC_3	concentration required to induce a threshold positive sensitization response (SI=3)
EDD	estimated daily dose
EDE	estimated daily exposure
EEC	estimated environmental concentration
EPI	Estimation Programs Interface
ER_{25}	effective rate for 25% of the population

ER_{50}	effective rate for 50% of the population
FIR	Food Ingestion Rate
g	gram(s)
GABA	gamma-aminobutyric acid
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
HH	handheld
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
HtM	hand-to-mouth
ICE	isolated chicken eye
ICS	isocycloseram
IRAC	Insecticide Resistance Action Committee
IUPAC	International Union of Pure and Applied Chemistry
JIY	chlorantraniliprole
kg	kilogram(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 causing 50% mortality of the test population
LD_{50}	lethal dose causing 50% mortality of the test population
LLNA	local lymph node assay
Ln	Log normal
LOC	level of concern
LOD	limit of detection/determination
LOEC	lowest observed effect concentration
LOED	lowest observed effect dose
LOEL	lowest observed effect level
LOQ	limit of quantitation
LR_{50}	lethal rate on 50% of the population
m^2	square metre(s)
m^3	cubic metre(s)
MAS	maximum average score
MIS	maximum irritation score
mg	milligram(s)
mL	millilitre(s)
M/L/A	mixer/loader/applicator
MOA	mode of action
MOE	margin of exposure
mol	mole
MPHG	mechanically pressurized handgun
MPHW	mechanically pressurized hand wand
MRL	maximum residue limit
N/A	not applicable
NAFTA	North American Free Trade Agreement
ND	not detected

nm	nanometres
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEDD	no observed effect dietary dose
NOEL	no observed effect level
OECD TG	Organisation for Economic Co-operation and Development test guideline
ORETF	Outdoor Residential Exposure Task Force
OtM	object-to-mouth
Pa	Pascal(s)
PCPA	*Pest Control Products Act*
PHED	Pesticide Handlers Exposure Database
PHI	pre-harvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
Ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PWC	pesticide water calculator
PYO	pick-your-own
R	correlation coefficient
R^2	coefficient of determination
RAC	raw agricultural commodity
RD	residue definition
REI	restricted-entry interval
RQ	risk quotient
SDEV	standard deviation
SPN	science policy note
SU	suspension
TC	transfer coefficient
TGAI	technical grade active ingredient
TP	transformation product
TSMP	Toxic Substances Management Policy
TTR	turf transferable residue
UCL	upper certified limit
UF	uncertainty factor
U.S.	United States
USEPA	United States Environmental Protection Agency
w/w	weight for weight

Appendix I Tables and figures

Table 1 Required personal protective equipment for EQUENTO RFC

Seed types	Tasks	PPE/Engineering controls
For commercial seed treatment (facilities and mobile treaters)		
Lentils	Mixing, loading, treating and calibrating	Open or closed transfer. Long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes.
	Bagging, sewing seed bags, stacking and driving a forklift, cleaning and repair	Coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes.
For on-farm seed treatment and planting of treated seeds		
Lentils	Mixing, loading, treating, calibrating, cleaning, repairing, planting and any other activities involving handling treated seeds	Open or closed transfer. Long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes.
For planting commercially treated seeds		
Lentils	Handling and planting	Long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Use a closed-cab tractor when planting. Gloves are not required within the closed cab.

Table 2 Toxicology reference values for use in health risk assessment for isocycloseram*

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or Target MOE
Acute dietary females 13-49 years old	Developmental toxicity study in rats	Developmental NOAEL = 7.5 mg/kg bw/day **Corrected = 6.5 mg/kg bw/day** Malformations in the absence of maternal toxicity	1000
ARfD (females 13-49 years old) = 0.007 mg/kg bw			
Acute dietary infants and children <12 years old	Reproductive toxicity study in rats	Offspring NOAEL = 4.1 mg/kg bw/day **Corrected = 3.5 mg/kg bw/day** Decreased viability in the presence of parental toxicity	300
ARfD (infants and children <12 years old) = 0.012 mg/kg bw			
Acute dietary youth 12-16 years old and adults 16+ years old	90-day oral toxicity study in dogs	NOAEL = 15 mg/kg bw/day **Corrected = 13 mg/kg bw/day** ↓ bw/bwg (week 1)	100
ARfD (youth 12-16 years old and adults 16+ years old) = 0.13 mg/kg bw			
Repeated (chronic) dietary	Developmental toxicity study in rats	Developmental NOAEL = 7.5 mg/kg bw/day **Corrected = 6.5 mg/kg bw/day** Malformations in the absence of maternal toxicity	1000
ADI = 0.007 mg/kg bw/day			
Occupational: Dermal[2] and inhalation[3] (all durations)	Developmental toxicity study in rats	Developmental NOAEL = 7.5 mg/kg bw/day **Corrected = 6.5 mg/kg bw/day** Malformations in the absence of maternal toxicity	1000
Residential: Dermal and incidental oral (all durations) (children 1 to <2 years old)	Reproductive toxicity study in rats	Offspring NOAEL = 4.1 mg/kg bw/day **Corrected = 3.5 mg/kg bw/day** Decreased viability in the presence of parental toxicity	300
Residential: Dermal (all durations) (children 6 to <11 years old)	Reproductive toxicity study in rats	Offspring NOAEL = 4.1 mg/kg bw/day **Corrected = 3.5 mg/kg bw/day** Decreased viability in the presence of parental toxicity	300

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or Target MOE
Residential: Dermal (all durations) (youth 11 to <16 years old, adults 16+ years old)	Developmental toxicity study in rats	Developmental NOAEL = 7.5 mg/kg bw/day **Corrected = 6.5 mg/kg bw/day** Malformations in the absence of maternal toxicity	1000
Aggregate residential: Dermal and oral (all durations) (children 1 to <2 years old; and children 6 to <11 years old)	Dermal and oral: Reproductive toxicity study in rats	Common endpoint: Decreased offspring viability in the presence of parental toxicity Dermal and oral: Offspring NOAEL = 4.1 mg/kg bw/day **Corrected = 3.5 mg/kg bw/day**	Dermal and oral: 300
Aggregate residential: Dermal and oral (all durations) (youth 11 to <16 years old, adults 16+ years old)	Dermal and oral: Developmental toxicity study in rats	Common endpoint: Malformations in the absence of maternal toxicity Dermal and oral: Developmental NOAEL = 7.5 mg/kg bw/day **Corrected = 6.5 mg/kg bw/day**	Dermal and oral: 1000
Cancer	Equivocal increase in Leydig cell tumours in rats (low level of concern to humans). Equivocal increase in ovarian luteomas in mice. Toxicology reference values selected for non-cancer risk assessment are protective of any residual concerns regarding carcinogenic potential.		

* The selected points of departure were corrected for the concentration of isomer SYN548088 within Isocycloseram Technical, as well as for the purity of Isocycloseram Technical, up to the UCL for both (in other words, 100%) as indicated on the submitted specification forms, to achieve the stated reference values.

1 CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE (margin of exposure) refers to a target MOE for occupational and residential assessments.

2 Since an oral NOAEL was selected, a dermal absorption factor of 8% was used in a route-to-route extrapolation.

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

Table 3 Toxicity profile of end-use products containing isocycloseram

Effects are known or assumed to occur in both sexes unless otherwise noted.

Study type/Animal/PMRA No.	Study results
A21377 CP	
Acute Oral Toxicity (Up and Down) Wistar rat PMRA No. 3246339	LD_{50} > 5000 mg/kg bw (♀) Clinical signs included irritability, hunched back, and piloerection. Low acute oral toxicity
Acute Dermal Toxicity Wistar rat PMRA No. 3246340	LD_{50} > 5000 mg/kg bw (♂/♀) Females exhibited hunched back and piloerection. Low acute dermal toxicity
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rat PMRA No. 3246343	LC_{50} > 5.13 mg/L (♂/♀) Males exhibited irregular respiration. Females exhibited hypoactivity, irregular respiration, nasal discharge, anogenital staining, hunched posture and hypersensitivity. Low acute inhalation toxicity
Eye Irritation New Zealand white rabbit PMRA No. 3246346	MAS = 0 MIS = 9.33/110 at 1 hour Non-irritating to the eye
Eye Irritation (In vitro ICE) Ross 308 chicken eyes PMRA No. 3246347	Overall ICE class = 3 × Class I Non-irritant to the eye according to OECD TG 438

Study type/Animal/PMRA No.	Study results
Dermal Irritation New Zealand white rabbit PMRA No. 3246345	MAS = 0 MIS = 0 Non-irritating to the skin
Dermal Irritation (In vitro EpiSkin™) Reconstructed human epidermis (EpiSkin™) PMRA No. 3246344	Relative tissue viability = 79.7% Non-irritant to the skin according to OECD TG 439
Sensitization (LLNA) CBA/J mouse PMRA No. 3246348	Negative
A21708 CP	
Acute Oral Toxicity (Up and Down) Sprague-Dawley rat PMRA No. 3246554	2000 mg/kg bw < LD_{50} < 5000 mg/kg bw (♀) Clinical signs included hypoactivity, irregular respiration, hunched posture, piloerection, reduced fecal volume, and slight tremors. Low acute oral toxicity
Acute Dermal Toxicity PMRA No. 3246555	The requirement for this study has been waived on the basis that this study is no longer a routine data requirement. The acute oral hazard category was used as an alternative for predicting dermal hazard. A21708 CP is considered to be of low acute dermal toxicity based on the acute oral toxicity study results.

Study type/Animal/PMRA No.	Study results
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rat PMRA No. 3246556	LC_{50} > 5.31 mg/L (♂/♀) Clinical signs included irregular respiration and moist rales. Low acute inhalation toxicity
Eye Irritation New Zealand white rabbit PMRA No. 3246559	MAS = 10/110 MIS = 18.7/110 at 24 hours Mildly irritating to the eyes All effects resolved by Day 7
Eye Irritation (In vitro ICE) Ross 308 chicken eyes PMRA No. 3246560	Overall ICE class = 1 × Class I, 1 × II, 1 × IV Not a severe irritant and not a non-irritant according to OECD TG 438
Dermal Irritation New Zealand albino rabbit PMRA No. 3246557	MAS = 0 MIS = 0 Non-irritating to the skin
Dermal Irritation (In vitro EpiDerm™) Reconstructed human epidermis (EPI-200-SIT) PMRA No. 3246558	Relative tissue viability = 79.8% Non-irritant to the skin according to OECD TG 439

Study type/Animal/PMRA No.	Study results
Sensitization (LLNA) CBA/J mouse PMRA No. 3246561	Positive EC_3 = 72% Potential dermal sensitizer
A22466 CP	
Acute Oral Toxicity (Up and Down) Sprague-Dawley rat PMRA No. 3246710	LD_{50} > 5000 mg/kg bw (♀) Clinical signs included hypoactivity, irregular respiration, ataxia, and reduced fecal volume. Low acute oral toxicity
Acute Dermal Toxicity PMRA No. 3246711	The requirement for this study has been waived on the basis that this study is no longer a routine data requirement. The acute oral hazard category was used as an alternative for predicting dermal hazard. A22466 CP is considered to be of low acute dermal toxicity based on the acute oral toxicity results.
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rat PMRA No. 3246712	LC_{50} > 5.20 mg/L (♂/♀) Clinical signs included hypoactivity, irregular respiration, anogenital staining, and hunched posture. Low acute inhalation toxicity
Eye Irritation PMRA No. 3246716	The requirement for this in vivo study has been waived based on the results of the in vitro eye irritation study. A22466 CP is considered to be corrosive to the eye.

Study type/Animal/PMRA No.	Study results
Eye Irritation (In vitro ICE) Ross 308 chicken eyes PMRA No. 3246715	Overall ICE class = 1 × Class I, 2 × III; severe loosening of epithelium (1 eye) Moderate corneal opacity (3 eyes) and moderate fluorescein retention change (3 eyes) noted at 4 hours in eyes treated with the test material. The test material was stuck on cornea surfaces (2 eyes) after the post-treatment rinse. Surfaces cleared at 120 or 180 minutes following the post-treatment rinse. Loosening of the epithelium (2 eyes) at 30 minutes after the post-treatment rinse. Severe loosening of epithelium (1 eye) at 75 minutes (changing to slight at 30 minutes) following the post-treatment rinse. Severe irritant to the eye according to OECD TG 438
Dermal Irritation New Zealand albino rabbit PMRA No. 3246714	MAS = 0 MIS = 0.7/8 at 1 hour Non-irritating to the eye
Dermal Irritation (In vitro EpiSkin™) Reconstructed human epidermis (EpiSkin™) PMRA No. 3246713	Relative tissue viability = 82.6% Non-irritant to the skin according to OECD TG 439
Sensitization (LLNA) CBA/J mouse PMRA No. 3246717	Positive EC_3 (extrapolated) = 21.60% Potential skin sensitizer

Study type/Animal/PMRA No.	Study results
EQUENTO RFC	
Acute Oral Toxicity (Up and Down) Sprague-Dawley rat PMRA No. 3246771	LD_{50} > 5000 mg/kg bw (♀) No effects noted. Low acute oral toxicity
Acute Dermal Toxicity PMRA No. 3246772	The requirement for this study has been waived on the basis that this study is no longer a routine data requirement. The acute oral hazard category was used as an alternative for predicting dermal hazard. EQUENTO RFC is considered to be of low acute dermal toxicity based on the acute oral toxicity results.
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rat PMRA No. 3246773	LC_{50} > 5.15 mg/L (♂/♀) Clinical signs included irregular respiration and anogenital staining. Low acute inhalation toxicity
Eye Irritation New Zealand albino rabbit PMRA No. 3246777	MAS = 0.7/110 MIS = 3.3/110 at 1 hour Minimally irritating to the eye
Eye Irritation (In vitro ICE) Ross 308 chicken eyes PMRA No. 3246776	Overall ICE class = 2 × Class II, 1 × III Not a severe irritant and not a non-irritant to the eye according to OECD TG 438

Study type/Animal/PMRA No.	Study results
Dermal Irritation New Zealand albino rabbit PMRA No. 3246775	MAS = 0.3/8 MIS = 1.0/8 at 1 hour Minimally irritating to the skin
Dermal Irritation (In vitro EpiDerm™) Reconstructed human epidermis (EPI-200-SIT) PMRA No. 3246774	Relative tissue viability = 102.6% Non-irritant to the skin according to OECD TG 439
Sensitization (LLNA) CBA/J mouse PMRA No. 3246778	Negative
A23294 TO	
Acute Oral Toxicity (Up and Down) Sprague-Dawley rat PMRA No. 3246941	LD_{50} > 5000 mg/kg bw (♀) No effects noted. Low acute oral toxicity
Acute Dermal Toxicity PMRA No. 3246942	The requirement for this study has been waived on the basis that this study is no longer a routine data requirement. The acute oral hazard category was used as an alternative for predicting dermal hazard. A23294 TO is considered to be of low acute dermal toxicity based on the acute oral toxicity results.

Study type/Animal/PMRA No.	Study results
Acute Inhalation Toxicity (nose-only) Sprague-Dawley rat PMRA No. 3246943	LC_{50} > 5.14 mg/L (♂/♀) Clinical signs included irregular respiration, moist rales, anogenital staining, hypoactivity, and hunched posture. Low acute inhalation toxicity
Eye Irritation New Zealand albino rabbit PMRA No. 3246946	MAS = 0.7/110 MIS = 3.3/110 at 1 hour Minimally irritating to the eye
Eye Irritation (In vitro ICE) Ross 308 chicken eyes PMRA No. 3246947	Overall ICE class = 3 × Class I Non-irritant to the eye according to OECD TG 438
Dermal Irritation New Zealand albino rabbit PMRA No. 3246944	MAS = 0 MIS = 0 Non-irritating to the skin
Dermal Irritation (In vitro EpiDerm™) Reconstructed human epidermis (EPI-200-SIT) PMRA No. 3246945	Relative tissue viability = 82.3% Non-irritant to the skin according to OECD TG 439

Study type/Animal/PMRA No.	Study results
Sensitization (LLNA) CBA/J mouse PMRA No. 3246948	Negative

Table 4a AHETF/PHED unit exposure estimates for mixers, loaders and applicators handling A21377 CP, A21708 CP and A22466 CP (µg/kg a.i. handled)

Exposure scenario and PPE	Dermal	Dermal (adjusted)[1]	Inhalation[2]
PPE: Single layer and chemical-resistant gloves			
Mixer/loader AHETF estimates			
Open Mix/Load Liquids	58.50	4.68	0.63
Applicator AHETF estimates			
Open Cab Groundboom Liquid Application	25.40	2.03	1.68
Open Cab Airblast Liquid Application - Without CR Hat	3769.3	301.54	9.08
Mixer/Loader/Applicator PHED estimates			
Liquid, open pour, mechanically pressurized handgun (MPHG)	5585.49	446.8329	151
Liquid, open pour, backpack sprayer (BP)	5445.85	435.668	62.1
Liquid, open pour, manually pressurized hand wand (MPHW)	943.37	75.4696	45.2
Mixer/loader + applicator AHETF estimates			
Open Mix/Load Liquids + Open Cab Groundboom	83.90	6.71	2.31
Open Mix/Load Liquids + Open Cab Airblast - Without CR Hat	3827.80	306.22	9.71

[1] Adjusted with the dermal absorption value of 8%

[2] Light inhalation rate (except for backpack – moderate inhalation rate)

Table 4b Mixer/Loader/Applicator risk assessment for A21377 CP, A21708 CP and A22466 CP

Use	Application method	Rate	ATPD[1]	Exposure (µg/kg bw/day)[2]		MOE[3]		
				Dermal	Inhalation	Dermal	Inhalation	Combined[4]
Single Layer, CR Gloves (MLA)								
A21377 CP and A21708 CP								
Fruiting vegetables	Groundboom (Custom)	0.03 kg/ha	26 ha	0.065	0.023	99 300	289 000	73 900
Corn (field, seed, pop)	Groundboom (Custom)	0.03 kg/ha	140 ha	0.35	0.12	18 400	53 600	13 700
Pome fruits	Airblast	0.03 kg/ha	20 ha	2.30	0.073	2830	89 300	2740
Pome fruits	HH-MPHG	0.075 g/L[5]	3800 L	1.59	0.54	4080	12 100	3050
Pome fruits	HH-MPHW	0.075 g/L	150 L	0.011	0.0064	612 000	1 020 000	383 000
Pome fruits	HH-Backpack	0.075 g/L	150 L	0.061	0.0087	106 000	744 000	92 900
Soybeans	Groundboom (Custom)	0.03 kg/ha	360 ha	0.91	0.31	7170	20 800	5340
A22466 CP								
Corn (field, seed, pop)	Groundboom (Custom)	0.15 kg/ha	140 ha	1.76	0.61	3690	10 700	2700
Corn (field, seed, pop)	Groundboom (Farmer)	0.15kg/ha	80 ha	1.01	0.35	6460	18 800	4800

ATPD = Area Treated Per Day, MOE = Margin of Exposure, MLA = Mixer/Loader/Applicator, CR = Chemical Resistant, HH=Handheld, MPHG = Mechanically Pressurized Handgun, MPHW = Manually Pressurized Hand wand

1 Default ATPD

2 Exposure (µg/kg bw/day) = [(Unit exposure values (µg/kg a.i. handled) × ATPD (ha/day) × Rate (kg a.i. /ha)] / (80 kg bw) – or – [(Unit exposure values (µg/kg a.i. handled) × ATPD (L/day) × Rate (g a.i./L)] / (80 kg bw × 1000 g/kg)

3 Based on NOAEL (dermal and inhalation) = 6.5 mg/kg bw/day = 6500 µg/kg bw/day; Target MOE = 1000

4 Combined MOE = 1/[(1/dermal MOE)+(1/inhalation MOE)

5 Application rate for handheld equipment (g a.i./L): Maximum TGAI rate = 0.030 kg a.i./ha × 1000 g/kg/ (Minimum Spray Volume of 400 L/ha) = 0.075 g a.i./ L

Table 4c Summary of commercial seed treatment exposure studies used for lentils for EQUENTO RFC

Study	Crops assessed	PPE	Activity	Unit exposure values (µg/kg a.i.)	
				Dermal	Inhalation
Commercial open transfer application					
Krolski, 2006 (AH803) (Study: PMRA No. 2313625; Review: PMRA No. 1676917 and 2884534)	Wheat	Open M/L, single layer + socks, leather boots, rubber/latex gloves, and a hat	mixing, loading and operation	265.7	2.47
Krolski, 2010 (AH806), Study: PMRA No. 2313618 Review: PMRA No. 2074087 Updated memo: PMRA No. 2500931	Canola	Single layer + CR gloves. Coveralls	bagging, sewing, stacking and forklift	7.33	1.5
		Single layer + CR gloves, Coveralls	cleaning (clean-out activities)	56.2 µg/g a.i./100 kg seed	12.7 µg/g a.i./100 kg seed

PPE = personal protective equipment; single layer = long-sleeved shirt, long pants; M/L = mixing/loading; CR = chemical-resistant

Table 4d Commercial seed treatment exposure and risk assessment for EQUENTO RFC

Crop	Activity	Application rate (g a.i./kg seed)	Throughput[1] (kg seed/day)	Unit exposure values (µg/kg a.i.)		Exposure[2] (mg/kg bw/day)		MOE (Target =1000)		
				Dermal	Inhalation	Dermal	Inhalation	Dermal[3]	Inhalation[3]	Combined[4]
Krolski, 2006 (AH803) - Open M/L, Single layer + socks, leather boots, rubber/latex gloves, and a hat										
Lentils	mixing, loading and operation	0.05	98 000	265.7	2.47	0.00130	0.000151	4993	42 965	4473
Krolski, 2010 (AH806) – Coveralls over Single layer, CR gloves										
Lentils	Cleaning (clean-out activities)	5.00 g a.i./100 kg seed	Not applicable	56.2 µg/g a.i./100 kg seed	12.7 µg/g a.i./100 kg seed	0.00028	0.000794	23 132	8189	6048
	bagging, sewing, stacking and forklift	0.05	98000	7.33	1.5	0.00004	0.000092	180 973	70 748	50 864

1 Default throughput for lentils

2 Exposure (excluding cleaners) = (application rate × kg/1000 g × throughput) × unit exposure values × Absorption (8% for dermal and 100% for inhalation)/80 kg body weight × 1000 µg/mg
Cleaner Exposure = application rate (g a.i./100 kg seed) × unit exposure values (µg a.i./ g a.i./100 kg seed) × Absorption (8% for dermal and 100% for inhalation)/80 kg body weight × 1000 µg/mg

3 Based on a NOAEL (all durations) of 6.5 mg/kg bw/day and a target MOE of 1000. MOE = NOAEL/exposure.

4 Combined MOE = 1/[(1/dermal MOE)+(1/inhalation MOE)].

Table 4e Summary of on-farm seed treatment exposure studies used for lentils for EQUENTO RFC

Study	Crop assessed	PPE	Activity	Unit exposure values (µg/kg a.i.)	
				Dermal	Inhalation
On-Farm Treatment and Planting					
Krolski, 2006 (AH803) (Study: PMRA No. 2313625; Review: PMRA No. 1676917 and 2884534)	Wheat	Open M/L, single layer, CR gloves, closed cab planter	Treating, loading, planting	254.35	13.03

Table 4f On-farm seed treatment exposure and risk assessment for EQUENTO RFC

Crop	Activity	Application rate (g a.i./kg seed)	Throughput[1] (kg seed/day)	Unit exposure values (µg/kg ai)		Exposure[2] (mg/kg bw/day)		MOE (Target =1000)		
				Dermal	Inhalation	Dermal	Inhalation	Dermal[3]	Inhalation[3]	Combined[4]
On-farm treatment and planting										
Krolski, 2006 (Wheat) - Open mix/load, closed cab planter, wearing single layer, CR gloves										
Lentils	Treating, loading, planting	0.05	6000	254.35	13.03	0.00008	0.00005	85184	13 3026	51930

1 Default throughput for lentils
2 Exposure = (application rate × kg/1000 g × throughput) × unit exposure values × Absorption (8% for dermal and 100% for inhalation) /80 kg body weight × 1000 µg/mg
3 Based on a NOAEL (all durations) of 6.5 mg/kg bw/day and a target MOE of 1000. MOE = NOAEL/exposure.
4 Combined MOE = 1/[(1/dermal MOE)+(1/inhalation MOE)].

Table 4g AHETF/ORETF/PHED unit exposure estimates for mixer/loaders and applicators handling A23294 TO (µg/kg a.i. handled)

Exposure Scenario and PPE	Dermal	Dermal (adjusted)[1]	Inhalation[2]
PPE: SL and CR gloves			
Mixer/loader AHETF estimates			
Open Mix/Load Liquids	58.5	4.68	0.63
Applicator AHETF estimates			
Open Cab Groundboom Liquid Application	25.40	2.03	1.68
Applicator PHED estimates			
Liquid, open pour, mechanically pressurized handgun (MPHG)	5585.49	446.8392	151
Liquid, open pour, backpack sprayer (BP)	5445.85	435.668	62.1
Liquid, open pour, manually pressurized hand wand (MPHW)	943.37	75.4696	45.2
Mixer/loader + applicator AHETF/ORETF estimates			
Open Mix/Load Liquids + Open Cab Groundboom Liquid Application	83.9	6.71	2.31
M/L/A Handgun Lawn Sprayer (Liquid Flowable), PPE: Long pants, long sleeves, gloves	785	62.8	4.0

[1] Adjusted with the dermal absorption value of 8%
[2] Light inhalation rate (except for backpack – moderate inhalation rate)

Table 4h Mixer/loader/applicator risk assessment for A23294 TO

Use	Application Method	Rate	ATPD[1]	Exposure (µg/kg bw/day)[2]		MOE[3]		
				Dermal	Inhalation	Dermal	Inhalation	Combined[4]
Single Layer, CR Gloves (MLA)								
Greenhouse Ornamentals	HH-MPHG	0.000103 kg a.i./L	3800 L	2.19	0.739	2900	8800	2200
	HH-Backpack	0.000103 kg a.i./L	150 L	0.084	0.012	77300	542000	67600
	HH-MPHW	0.000103 kg a.i./L	150 L	0.015	0.0087	44600	744600	279000
Turf and Sod*	Groundboom	0.05 kg a.i. /ha	30 ha	0.1258	0.043	51650	150070	38400
	Turf Gun Sprayer	0.05 kg a.i. /ha	2 ha	0.0785	0.0050	82800	1300000	77850

ATPD = Area Treated Per Day, MOE = Margin of Exposure, MLA = Mixer/Loader/Applicator, CR = Chemical-resistant, HH = Handheld, MPHG = Mechanically Pressurized Handgun, MPHW = Manually Pressurized Hand wand
*Turf and sod risk assessment covers golf courses
[1] Default Area Treated per Day/Amount Handled per Day table
[2] Exposure (µg/kg bw/day) = Unit exposure value (µg/kg a.i. handled from Table 4g) × ATPD (ha/day) or AHPD (L/day) × Rate (kg a.i./ha or kg a.i./L) / (80 kg bw)
[3] Based on NOAEL (dermal and inhalation) = 6.5 mg/kg bw/day (6500 µg/kg bw/day); Target MOE (dermal and inhalation) = 1000
[4] Combined MOE = 1/[(1/dermal MOE)+(1/inhalation MOE)].

Table 5a Adjusted average dislodged residues: Apples

Sampling Interval[1]	Isocycloseram Residues (µg/cm^2)[2,3,4]		
	Trial TK0277342-01	Trial TK0277342-02	Trial TK0277342-03
	Pennsylvania Site	Illinois Site	California Site
Pre-Application 1(0DBA1)	<LOD	<LOD	0.0000935
Post-Application 1 (0DAA1)	0.07621	0.0963	0.0836
Pre-Application 2 (0DBA2)	0.08269	0.0859	0.0732
Post- Application 2 (0DAA2)	0.20151	0.1802	0.2083
Pre-Application 3 (0DBA3)	0.15647	0.0919	0.2659
Post-Application 3 (0DAA3)	0.20784	0.2263[8]	0.2758
1 DAA3	0.20981[8]	0.1591	0.2446
2 or 3 DAA3	0.20310	0.1336	0.3319[8]
7 or 8 DAA3	0.17109	0.1246	0.2344
9 or 10 DAA3	0.19006	0.1222	0.2116
13 or 14 DAA3	0.12483	0.1091	0.2388
21 or 22 DAA3	0.17662	0.1131	0.2189
28 DAA3	0.14658	0.0670	0.2296
33 - 35 DAA3	0.13987	0.0590	0.1649
Calculated half-life (days)	62	22	59
Average Adjusted Peak SYN54707 Residue (µg/cm^2) (SD)	0.21 (0.01)	0.226 (0.06)	0.332 (0.002)
Total Application Rate (kg a.i./ha)	0.271	0.278	0.270
Application Rate (kg a.i./ha)	0.090	0.093	0.091
Application Rate (µg a.i./cm^2)[5]	0.90	0.93	0.91
Percent (%) Peak dislodgeable residues (DAA1)[6]	8.4	10.4	9.4

Sampling Interval[1]	Isocycloseram Residues (µg/cm²)[2,3,4]		
	Trial TK0277342-01	Trial TK0277342-02	Trial TK0277342-03
	Pennsylvania Site	Illinois Site	California Site
Percent (%) Peak dislodgeable residues (DAA2)[6]	22.4	19.6	23.1
Percent (%) Peak dislodgeable residues (DAA3)[6]	23.1	24	30.3
Dissipation rate per day (%)[7]	1.1	3.0	1.2

Average dislodged residues were adjusted: field trial samples were adjusted for low fortification recoveries in other words, the midpoint value for mean fortification recoveries were calculated and then used in adjusting field trial samples recoveries.

1 DBA = days before application; DAA = days after application; DAA3 = days after application 3 (last application); SD = standard deviation
2 Average of three treated subplots.
3 Limit of quantitation (LOQ) = 0.05 µg/L; equivalent to 0.000025 mg/cm²
4 Adjusted for field fortification recovery results.
5 Conversion of Application Rate (kg a.i./ha to µg a.i./cm²): (rate kg a.i./ha × 1000 g/kg × 1000 mg/g × 1000 µg/mg × 1 ha)/100 000 000 cm²
6 Percent (%) dislodgeable residues = Residue (average adjusted residue (µg/cm²)) ÷ single application rate (µg a.i./cm²) × 100%
7 Dissipation rate per day = 1 - EXP(Slope) * 100
8 Peak isocycloseram residues

Table 5b Average adjusted dislodged residues: Tomatoes

Sampling interval[1]	Isocycloseram residues (µg/cm²)[2,3,4]		
	Site TK0384494-01	Site TK0384494-02	Site TK0384494-03
	Pennsylvania site	Georgia site	California site
Pre-application 1 (0DBA1)	<LOD	<LOD	<LOD
Postapplication 1 (0DAA1)	0.2496	0.2674	0.2288
Pre-application 2 (0DBA2)	0.12735	0.1670	0.2185
Postapplication 2 (0DAA2)	0.5004[8]	0.3405	0.2941
Pre-application 3 (0DBA3)	0.26905	0.2273	0.3152
Postapplication 3 (0DAA3)	0.47540	0.5856[8]	0.4593[8]
1 DAA3	0.44841	0.3345	0.3944
3 or 4 DAA3	0.200	0.2004	0.4593
7 DAA3	0.1384	0.1485	0.2074
9 or 10 DAA3	0.10241	0.2205	0.2829
13 or 14 DAA3	0.04120	0.1505	0.4085
21 or 22 DAA3	0.00986	0.0667	0.0836

Sampling interval[1]	Isocycloseram residues (µg/cm^2)[2,3,4]		
	Site TK0384494-01	Site TK0384494-02	Site TK0384494-03
	Pennsylvania site	Georgia site	California site
28 DAA3	0.00341	0.0734	0.0391
33–35 DAA3	0.00309	0.1087	0.0279
Calculated half-life (days)	15	14	8
Average adjusted peak SYN54707 Residue (µg/cm^2) (SD)/Sampling interval	0.500 (0.028)/0DAA2	0.586 (0.093)/0DAA3	0.460 (0.21)/0DAA3
Total application rate (kg a.i./ha)	0.367	0.363	0.363
Application rate (kg a.i./ha)	0.120	0.121	0.122
Application rate (µg a.i./cm^2)[5]	1.20	1.21	1.22
Percent (%) Peak dislodgeable residues (DAA1)[6]	20.13	22.1	18.9
Percent (%) Peak dislodgeable residues (DAA2)[6]	41.7	28.1	24.5
Percent (%) Peak dislodgeable residues (DAA3)[6]	38.7	48.4	37.65
Dissipation rate per day (%)[7]	14.74	4.73	7.97

1 DBA = days before application; DAA = days after application; DAA3 = days after application 3 (last application); SD = standard deviation
2 Average of three treated subplots.
3 Limit of quantitation (LOQ) = 0.05 µg/L; equivalent to 0.000025 mg/cm^2
4 Adjusted for field fortification recovery results.
5 Conversion of Application Rate (kg a.i./ha to µg a.i./cm^2): (rate kg a.i./ha × 1000 g/kg × 1000 mg/g × 1000 µg/mg × 1 ha)/100,000,000 cm^2
6 Percent (%) dislodgeable residues = Residue (average adjusted residue (µg/cm^2)) ÷ single application rate (µg a.i./cm^2) × 100%
7 Dissipation rate per day = 1 - EXP(Slope) * 100
8 Peak isocycloseram residues

Table 5c Summary of Turf Transferable Residue (TTR) Data for Isocycloseram

Application #	Sampling Interval (DAA)	Pennsylvania Site		Georgia Site		California Site	
		Residue (µg/cm^2)	Ln TTR [b]	Residue (µg/cm^2) [1]	Ln TTR [2]	Residue (µg/cm^2)	Ln TTR [2]
1	PRE	ND	ND	ND	ND	ND	ND
	0	0.0143	-4.25	0.00502	ND	0.00867	-4.75
2	PRE	0.00085	-7.06	0.000656	-7.33	0.00049	-7.63
	0	0.0121	-4.41	0.00531	-5.24	0.00910[11]	-4.70

Application #	Sampling Interval (DAA)	Pennsylvania Site		Georgia Site		California Site	
		Residue (µg/cm^2)	Ln TTR [b]	Residue (µg/cm^2) [1]	Ln TTR [2]	Residue (µg/cm^2)	Ln TTR [2]
	1	0.013[11]	-4.35	0.00543	-5.22	0.00786	-4.85
	3	0.0069	-4.98	0.00548[11]	-5.21	0.00720	-4.93
	7 (-1) [6]	0.00511	-5.28	0.00328	-5.72	0.00118	-6.74
	10	0.00133	-6.62	0.00316	-5.76	0.00111	-6.80
	14 (-1) [7]	0.00067	-7.31	0.00208	-6.18	0.00033	-8.03
	21 (-1) [8]	0.00023	-8.39	0.00143	-6.55	0.00009	-9.32
	28 (-1) [9]	0.00003	-10.52	0.00057	-7.47	0.00003	-10.52
	35 (-1) [10]	0.00003	-10.52	0.00035	-7.94	0.00003	-10.52
Correlation Coefficient		-0.8463	N/A	-0.9550	N/A	-0.8215	N/A
Peak TTR after 1st application (%) [3]		0.95		0.33		0.58	
Peak TTR after 2nd application (%) [3]		0.88		0.37		0.61	
Dissipation Rate (%/day) [4]		20		8		19	
Half-life (days) [5]		3		8		3	

TTR = transferable turf residue; PRE = previous to application; ND = not detected; N/A = not applicable; DAA = days after application

1 Residues were corrected where the corresponding field fortification recovery was <95%.

2 Natural log of the average isocycloseram TTR.

3 Peak TTR (%) was calculated by dividing isocycloseram residues by the study application rate expressed in µg/cm^2.

4 Calculated using the following equation: Dissipation rate = 1-e^{slope}.

5 Calculated using the following equation: Half-life = 0.693/slope.

6 Pennsylvania 6 DAA

7 Pennsylvania 13 DAA

8 Georgia 20 DAA

9 Pennsylvania and Georgia 27 DAA

10 Pennsylvania and Georgia 34 DAA

11 Peak isocycloseram residues

Table 6a Postapplication exposure and risk estimates to workers after 2 applications of A21377 CP and A21708 CP

Crops	Re-entry activities	Peak DFR (µg/cm^2)[1]	TC (cm^2/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI (days)
Tuberous and corm vegetables (potatoes) - CG 1C	Irrigation, hand set	0.08340	1750	0.00117	5567	0
Corn	Detasseling, hand	0.08340	8800	0.00587	1107	0
	Irrigation, handset	0.08340	1750	0.00117	5567	0
Leafy vegetables	Weeding, hand	0.08340	4400	0.00294	2214	0
	Irrigation, hand set	0.08340	1750	0.00117	5567	0
Brassica head and stem	Harvesting, hand	0.08340	5150	0.00344	1892	0
	Weeding, hand	0.08340	4400	0.00294	2214	0
Fruiting vegetables	Irrigation, hand set	0.08340	1750	0.00117	5567	0
	Harvesting, hand; pruning, hand	0.08340	1100	0.00073	8857	0
Cucurbit vegetables (smooth leaves)	Irrigation, hand set	0.08340	1750	0.00117	5567	0
Pome and Stone fruits	Thinning, hand	0.04480	3000	0.00108	6045	0
	Harvesting (hand)	0.04480	1400	0.00050	12954	0
Tree nuts	Pruning (hand), Scouting	0.04480	580	0.00021	31269	0
Soybean	Scouting	0.08340	1100	0.00073	8857	0

DFR = Dislodgeable foliar residue; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Restricted-Entry Interval

1 Calculated using the % peak DFR (after 2nd application) of 22.4% and 1% dissipation obtained from the apple study (Pennsylvania site), for pome fruits, stone fruits and tree nuts; for all other crops, used the % peak DFR of 41.7% obtained from the tomato study (after 2nd application) and the standard dissipation of 10% per day (outdoor scenarios).

2 Transfer coefficients obtained from PMRA Agricultural TCs Table

3 Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/hr] × 8 hours/day × [8 % dermal absorption]) / (80 kg bw × 1000 µg/mg)

4 Based on a NOAEL of 6.5 mg/kg bw/day; Target MOE = 1000

5 Minimum REI is 12 hours to allow residues to dry, suspended particles to settle and vapours to dissipate.

Table 6b Summary of seed planting exposure study used for isocycloseram on lentils for EQUENTO RFC

Study	Crops assessed	PPE	Activity	Unit exposure values (µg/kg a.i.)	
				Dermal	Inhalation
Planting commercially treated seed					
Zietz, 2007 (AH825) (Review: 2883441 (2ndary), 1630787 (original), 2222638 (2012 update) Study# 2313628	Corn	Single Layer + CR gloves, closed cab	Loading, planting, unloading remaining seed, repair	1606.9	80.88

PPE = personal protective equipment; single layer = long-sleeved shirt, long pants; M/L = mixing/loading; CR = chemical-resistant

Table 6c Planting commercially treated seed exposure and risk assessment for EQUENTO RFC

Crop	Form	Activity	Application rate (g a.i./kg seed)	Throughput[1] (kg seed/day)	Unit exposure values (µg/kg a.i.)		Exposure[2] (mg/kg bw/day)		MOE (Target =1000)		
					Dermal	Inhalation	Dermal	Inhalation	Dermal[3]	Inhalation[3]	Combined[4]
Zietz, 2007 (AH825) - closed cab planter, wearing single layer, CR gloves											
Lentils	Liquid	Loading, planting, unloading remaining seed, repair	0.05	6000	1606.9	80.88	0.000482	0.00030	13484	21431	8276

1 Default throughput

2 Exposure (excluding cleaners) = (application rate × kg/1000 g × throughput) × unit exposure values × Absorption (8% for dermal and 100% for inhalation) /80 kg body weight × 1000 µg/mg

3 Based on a NOAEL (all durations) of 6.5 mg/kg bw/day and a target MOE of 1000. MOE = NOAEL/exposure.

4 Combined MOE = 1/[(1/dermal MOE)+(1/inhalation MOE)].

Table 6d Postapplication exposure and risk estimates to workers after the last application – Turf (A23294 TO)

Postapplication activity	Application rate (µg/cm²)	Peak TTR (µg/cm²)[1]	TC (cm²/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI
Sod farms						
Slab harvesting and transplanting/planting	0.5	0.0048	6700	0.0003	25530	12 hours[5]
Golf courses						
Transplanting/planting, mowing, watering, cup changing, irrigation repair and miscellaneous grooming	0.5	0.0048	3500	0.0001	48872	Until sprays have dried

TTR = Turf Transferrable Residue; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Restricted-Entry Interval

1 Calculated using 0.95% of the application rate on Day 0 after the last application and 20% dissipation per day

2 Transfer coefficients obtained from PMRA Agricultural TCs Table

3 Exposure = (Peak TTR [µg/cm²] × TC [cm²/hr] × 8 hours/day × DAF (8%) / (80 kg bw × 1000 µg/mg)

4 Based on a NOAEL of 6.5 mg/kg bw/day; Target MOE = 1000

5 Minimum REI is 12 hours to allow residues to dry, suspended particles to settle and vapours to dissipate for sod farms. For golf courses, until sprays have dried is recommended.

Table 6e Postapplication worker exposure and risk estimate on day 0 after the last application – Greenhouse ornamentals (A23294 TO)

Crop	Use pattern	Postapplication activity	Peak DFR (µg/cm²)[1]	Transfer coefficient (TC) (cm²/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI[5]
Greenhouse ornamentals (excluding cut flowers)	1 app at 0.150 kg a.i./ha, using % peak DFR = 20.13%	All activities	0.3020	230	0.000556	11699	0
	2 app at 0.09 kg a.i./ha each (using % peak DFR = 41.7%), RTI = 7 days	All activities	0.3753	230	0.00069	9413	0

Crop	Use pattern	Postapplication activity	Peak DFR (µg/cm²)[1]	Transfer coefficient (TC) (cm²/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI[5]
Greenhouse ornamentals grown for cut flower production	1 app at 0.15 kg a.i./ha, using % peak DFR=20.13%	Hand pruning, disbudding, hand harvesting	0.3020	4000	0.00966	673	0
			0.2016	4000	0.00645	1008	20 days
	2 app at 0.09 kg a.i./ha each (using % peak DFR = 41.7%), RTI = 7 days	Hand pruning, disbudding, hand harvesting	0.3753	4000	0.01201	541	0
			0.2047	4000	0.0066	992	30 days
	A single app at 0.1 kg a.i./ha, using % peak DFR = 20.13%	Hand pruning, disbudding, hand harvesting	0.2013	4000	0.00644	1009	0
	A single app at 0.1 kg a.i./ha, using % peak DFR = 20.13%	Scouting, weeding (hand), transplanting, pinching, plant support	0.2013	230	0.0004	17548	0

DFR = Dislodgeable foliar residue; TC = Transfer Coefficient; MOE = Margin of exposure; REI = Restricted-entry interval

1 Calculated using % peak DFR from the tomato study of 41.7% and default 2% daily dissipation for the scenario with 2 applications at 0.09 kg a.i./ha; and % peak DFR of 20.13% and default 2% daily dissipation for the scenario with 1 application at 0.15 kg a.i./ha; % peak DFR of 20.13% was also used to model the mitigated risk assessment of a single application (0.1 kg a.i./ha) for greenhouse ornamentals grown for cut flower production.

2 Transfer coefficients obtained from PMRA Agricultural TCs Table

3 Exposure = (Peak DFR [µg/cm²] × TC [cm²/hr] × 8 hours/day × [8% dermal absorption]) / (80 kg bw × 1000 µg/mg)

4 Based on a NOAEL of 6.5 mg/kg bw/day, Target MOE = 1000

5 Minimum REI is 12 hours to allow residues to dry, suspended particles to settle and vapours to dissipate.

Table 7a Postapplication dermal exposure and risk estimates to residents on day 0 from residential orchard trees treated commercially with A21377 CP and A21708 CP

Crop (Max rate; # App; RTI)	Life stage	Peak DFR (µg/cm²)[1]	TC (cm²/hr)[2]	Exposure time (hr/day)	Dermal exposure (mg/kg bw/day)[3]	MOE[4]
Pome fruits	Adults (16+ years)	0.0448	1700	1	7.62E-05	85 350

Crop (Max rate; # App; RTI)	Life stage	Peak DFR ($\mu g/cm^2$)[1]	TC (cm^2/hr)[2]	Exposure time (hr/day)	Dermal exposure (mg/kg bw/day)[3]	MOE[4]
(0.02 kg a.i./ha; 2/season; 7-day RTI)*	Children (6 to < 11 years)		930	0.5	5.21E-05	67 i200

DFR = Dislodgeable foliar residue; TC = Transfer Coefficient; MOE = Margin of Exposure
*This covers stone fruits and tree nuts.
1 Based on DFR obtained from apple study
2 A single TC is representative of all activities in residential fruit trees. TCs were obtained from the 2012 USEPA SOP for Residential Pesticide Exposure Assessment.
3 Dermal Exposure = (Peak DFR [$\mu g/cm^2$] × TC [cm^2/hr] × Exposure duration [hours/day] × [8% dermal absorption]) / (Body weight [80 kg for adults; 32 kg for children (6 to <11 years)] × 1000 µg/mg)
4 NOAEL/Dermal Exposure; Based on a NOAEL of 6.5 mg/kg bw/day; Target MOE of 1000 for adults; NOAEL of 3.5 mg/kg bw/day; Target MOE of 300 for children (6 to <11 years)

Table 7b Dermal exposure and risk estimates to the general public from golf courses Treated with A23294 TO

Life stage	Peak TTR ($\mu g/cm^2$)[1]	TC (cm^2/hr)[2]	Exposure time (hr/day)	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI
Adult (16+ yrs)	0.0048	5300	4	0.00010176	64000	Until sprays have dried
Youth (11 to <16 yrs)	0.0048	4400	4	0.000118	55000	Until sprays have dried
Children (6 to <11 yrs)	0.0048	2900	4	0.000139	25000	Until sprays have dried

TTR = Turf Transferrable Residues; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Restricted-Entry Interval
1 Calculated using 0.95% of the application rate on Day 0 after the last application and 20% dissipation per day.
2 A single TC is representative of all activities on golf courses. TCs were obtained from the 2012 USEPA SOP for Residential Pesticide Exposure Assessment.
3 Dermal Exposure (mg/kg bw/day) = (Peak TTR [$\mu g/cm^2$] × TC [cm^2/hr] × Exposure Time [hours/day] × [8% dermal absorption]) / (Body weight [80 kg for adults; 57 kg for youth; 32 kg for children] × 1000 µg/mg)
4 Based on a NOAEL of: Adults (16+) and youth (11 to <16 years) = 6.5 mg/kg bw/day; Target MOE of 1000
Children (6 to < 11 years) = 3.5 mg/kg bw/day; Target MOE of 300

Table 7c Postapplication dermal exposure and risk estimates to residents from turf treated with A23294 TO

Life stage	Activity	Peak TTR (µg/cm^2)[1]	TC (cm^2/hour)[2]	Exposure time (hour/day)	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI
Adult (16+ years)	High Contact	0.0048	180 000	1.5	0.00129	5000	Until sprays have dried
	Mowing		5500	1	0.000026	250 000	Until sprays have dried
Youth (11 to <16 years)	Mowing		4500	1	0.00003	210 000	Until sprays have dried
Children (1 to <2 years)	High Contact		49000	1.5	0.00256	1400	Until sprays have dried

TTR = Turf Transferrable Residues; TC = Transfer Coefficient; MOE = Margin of Exposure; REI = Restricted-Entry Interval

1 Calculated using chemical specific TTR values of 0.95% of the application rate on Day 0 after the last application and [20%] dissipation per day.

2 TCs were obtain from 2012 Residential SOPs

3 Dermal Exposure (mg/kg bw/day) = (Peak TTR [µg/cm^2] × TC [cm^2/hr] × Exposure time [hours/day] × [8% dermal absorption]) / (Body weight [80 kg for adults; 57 kg for youth; 11 kg for children] × 1000 µg/mg)

4 Based on a NOAEL of: Adults (16+) and youth (11 to <16 years) = 6.5 mg/kg bw/day; Target MOE of 1000
Children (1 to < 2 years) = 3.5 mg/kg bw/day; Target MOE of 300

Table 7d Hand-to-mouth exposure and risk estimates to children following contact with turf treated with A23294 TO

Hand residue (mg/hr)	Fraction of hand surface area mouthed/event	Exposure time (hrs/day)	Number of replenishments/hr	Saliva extraction factor	Frequency (events/hr)	Oral exposure (mg/kg bw/day)	MOE[1]
0.00706	0.13	1.5	4	0.48	14	0.00011	31 000

MOE = Margin of Exposure

Refer to the 2012 USEPA SOP for Residential Pesticide Exposure Assessment for the exact algorithm

1 Based on a NOAEL of 3.5 mg/kg bw/day; Target MOE = 300

Table 7e Object-to-mouth exposure and risk estimates to children following contact with turf treated with A23294 TO

Object residue (µg/cm^2)	Object surface area mouthed/event (cm^2/event)	Exposure time (hrs/day)	Number of replenishments/hr	Saliva extraction factor	Frequency (events/hr)	Oral exposure (mg/kg bw/day)	MOE[1]
0.005	10	1.5	4	0.48	9	0.00002	170 000

OtM = Object-to-Mouth; N_Replen = Replenishment Interval per Hour; SEF = Saliva Extraction Factor; MOE = Margin of Exposure
Refer to the 2012 USEPA SOP for Residential Pesticide Exposure Assessment for the exact algorithm
[1] Based on a NOAEL of 3.5 mg/kg bw/day; Target MOE = 300

Table 8a Aggregate exposure and risk estimates for isocycloseram from residential orchard trees treated commercially with A21377 CP and A21708 CP

Life stage	Exposure (mg/kg bw/day)			MOE[4]
	Dermal[1]	Dietary[2]	Aggregate[3]	
Adult (16+ years)	0.0000762	0.000548	0.000624	10417
Children (6 to <11 years)	0.0000521	0.000758	0.000810	4321

MOE = Margin of Exposure
[1] Refer to Table 7a
[2] Chronic dietary (food + drinking water) exposure estimates
[3] Aggregate Exposure = Dermal Exposure + Dietary Exposure
[4] Aggregate MOE for adults = NOAEL of 6.5 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 1000
Aggregate MOE for children (6 to <11 years) = NOAEL of 3.5 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 300

Table 8b Aggregate Exposure and Risk Estimates for Golfers (A23294 TO)

Life Stage	Exposure (mg/kg bw/day)			MOE[4]
	Dermal[1]	Chronic Dietary[2]	Aggregate[3]	
Adults (16+ years)	0.00010176	0.000548	0.0006498	10 000
Youth (11 to <16 years)	0.0001185	0.000455	0.0005735	11 333
Children (6 to <11 years)	0.0001392	0.000758	0.0008972	3901

MOE = Margin of Exposure

[1] Postapplication dermal exposure from Table 5b

[2] Chronic dietary (food + drinking water) exposure estimates

[3] Aggregate exposure = Dermal Exposure + Chronic Dietary Exposure

[4] Aggregate MOE = NOAEL of 6.5 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 1000 (Youth (11 to <16 years); Adults (16+ years))
NOAEL of 3.5 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 300 (Children (6 to <11 years))

Table 8c Aggregate Exposure and Risk Estimates for Residents from Turf Treated with A23294 TO

Life Stage	Exposure (mg/kg bw/day)				MOE[5]
	Dermal[1]	Incidental oral[2]	Chronic dietary[3]	Aggregate[4]	
Adults (16+ years)	0.001296	Not applicable	0.000548	0.00184	3531
Children (1 to <2 years) (HtM Exposure)	0.00256	0.00011	0.001432	0.00399	878

MOE = Margin of Exposure

[1] Postapplication dermal exposure from Table 7c (High contact lawn activities)

[2] Hand-to-mouth exposure from Table 7d

[3] Chronic dietary (food + drinking water) exposure estimates

[4] Aggregate exposure = Dermal Exposure + Incidental Oral Exposure + Chronic Dietary Exposure

[5] Aggregate MOE = NOAEL of 6.5 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 1000 (Adults (16+ years))
NOAEL of 3.5 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 300 (Children (1 to < 2 years))

Table 9 Integrated food residue chemistry summary

Crop field trials and residue decline	**PMRA No. 3246058, 3246059, 3246061, 3246062, 3246063, 3246064, 3246065, 3246067, 3246068, 3246072, 3246074, 3246075, 3246080, 3246081, 3246089, 3246090**

Crop field trials were conducted in North American regions during the 2017 to 2019 growing seasons with a variety of crops using different formulated end-use products: SYN547407 SC (200 g/L; 400 g/L); SYN547407 DC (100 g/L); SYN547407 FS (100 g/L; 400 g/L). Application rates exceeded those approved on the domestic labels. Adjuvants were used in/on the various crops at all field trial sites. Different treatments were applied to various crops (foliar, in-furrow, seed treatment). The number and geographic distribution of trials were generally in accordance with Health Canada's SPN2017-02. Independence of trials was assessed for each representative crop from the various crop groups. Residue decline data show that quantifiable residues of isocycloseram decreased in the various crops with increasing pre-harvest intervals (PHIs). Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method.

Crop	**Total application rate (g a.i./ha)**	**PHI (days)**	**Isocycloseram residue levels (ppm)**					
			n	**LAFT**	**HAFT**	**Median**	**Mean**	**SDEV**
Potato tuber	176-189	13, 14	26	<0.01	<0.01	<0.01	<0.01	N/A
Leaf Lettuce	176-184	1	10	0.117	3.83	2.06	1.99	1.38
Mustard Greens	180-185	1	8	0.943	3.80	3.14	2.70	1.16
Spinach	179-188	1, 2	10	0.809	6.04	2.95	3.04	1.65
Cabbage With Wrapper Leaves	180-186	1	10	0.118	2.700	0.389	0.598	0.754
Broccoli	178-186	1	10	0.078	0.369	0.207	0.214	0.093
Cauliflower	179-186	1, 7	10	<0.010	0.282	0.051	0.088	0.090
Brussels Sprouts	180-184	1, 3	4	0.032	0.720	0.072	0.224	0.332
Soybean Forage	219-246 (SC)	13, 15	21	0.75	4.8	1.7	1.9	1.0
Soybean Hay		13, 15	21	1.5	12	5.5	5.9	2.6
Soybean Seed		12-25	21	<0.01	0.086	0.020	0.027	0.020
Soybean Forage	174-201 (DC)	13, 15	21	0.073	1.7	0.56	0.68	0.47
Soybean Hay		13, 15	21	0.56	4.8	1.6	2.0	1.3
Soybean Seed		12-25	21	<0.01	0.099	<0.01	0.015	0.020
Dry Bean	9.2-11.4 g a.i./100 kg seed	87-158	12	<0.01	<0.01	<0.01	<0.01	N/A
Dry Pea Hay	8.99-10.2 g a.i. 100 kg seed	41-62	8	<0.01	<0.01	<0.01	<0.01	N/A
Dry Pea Vines		41-62	8	<0.01	<0.01	<0.01	<0.01	N/A

Dry Pea Seed		84-109	8	<0.01	<0.01	<0.01	<0.01	N/A
Tomato	358-371	1, 2	16	0.016	0.362	0.101	0.121	0.085
Bell Pepper	358-378	1	8	0.037	0.144	0.095	0.095	0.036
Non-Bell Pepper	355-368	1	8	0.068	0.358	0.153	0.183	0.100
Eggplant	365-375	1	4	0.022	0.053	0.031	0.034	0.014
Cucumber	179-187	3	8	<0.01	0.056	0.024	0.027	0.017
Melon	182-185	3	8	0.011	0.068	0.032	0.036	0.020
Summer Squash	180-184	3	8	<0.01	0.060	0.012	0.019	0.017
Apple	268-278 (Dilute)	13, 15, 28	8	0.076	0.181	0.106	0.113	0.032
	251-273 (Concentrate)	13-15	9	0.040	0.200	0.112	0.103	0.050
Pear	265-277 (Dilute)	13, 14	6	0.057	0.241	0.110	0.122	0.062
	259-273 (Concentrate)	14, 28	6	0.052	0.210	0.148	0.141	0.071
Peach	266-274 (Dilute)	8, 13-14	6	0.059	0.270	0.151	0.158	0.071
	268-275 (Concentrate)	13-14, 20-21	7	0.037	0.119	0.084	0.081	0.027
Tart/Sweet Cherry	268-272 (Dilute)	14-15	5	0.270	0.420	0.380	0.372	0.061
	262-271 (Concentrate)	13-14	5	0.200	0.620	0.230	0.318	0.175
Plum	262-270 (Dilute)	13-14	5	0.024	0.112	0.093	0.079	0.038
	268-279 (Concentrate)	13-14, 21	5	0.010	0.229	0.055	0.079	0.089
Pecan Nutmeat	269-275	13, 15	5	<0.01	<0.01	<0.01	<0.01	N/A
Almond Nutmeat	269-271	13, 15	5	<0.01	0.083	<0.01	0.025	0.033
Almond Hulls	269-271	13, 15	5	0.330	3.07	1.21	1.48	1.021
Field Corn Forage In-furrow only	149-157	81-127	22	<0.01	<0.01	<0.01	<0.01	N/A
Field Corn Forage In-furrow + 2 Foliar	209-218	6-9	23	0.125	1.59	0.271	0.344	0.300

Field Corn Grain In-furrow + 2 foliar	209-218	19-22	23	<0.01	<0.01	<0.01	<0.01	N/A
Field Corn Stover In-furrow + 2 foliar	209-218	19-28	23	0.209	0.831	0.415	0.448	0.151
Popcorn Grain In-furrow + 2 foliar	211-216	20-21	4	<0.01	<0.01	<0.01	<0.01	N/A
Popcorn Stover In-furrow + 2 foliar	211-216	20-21	4	0.230	0.349	0.312	0.301	0.053
Peanut nutmeat	239-251	13-19	13	<0.01	<0.01	<0.01	<0.01	N/A
Peanut hay	239-251	13-19	13	0.426	3.73	1.82	1.83	1.02

n = number of independent trials; N/A: Not applicable, SC = Suspension concentrate; DC = Dispersible concentrate.
For computation, values <LOQ are assumed to be at the LOQ.

Processed food and feed - crop	**PMRA No. 3246061, 3246072, 3246073, 3246074, 3246075, 3246080, 3246081, 3246082, 3246083, 3246084, 3246085, 3246089, 3246090**

Processing studies were conducted in distinctive North American growing regions using A21708F DC, A21550L SC and A22241C FS at exaggerated rates (up to 23-fold cGAP) in/on almonds, apples, field corn, potatoes, peach, peanuts, plums, soybeans, spinach and tomatoes. Adequate storage stability data are available on diverse crop types to support the storage intervals of the processed food and feed. Samples were analyzed using a validated analytical method.

Isocycloseram residues in potatoes, field corn and peanuts were all <LOQ (<0.01 ppm) in the RAC and /or processed fractions for human consumption.

RAC	Processed fractions	HAFT$_{[RAC]}$ (ppm)	Average or median processing factor of isocycloseram	Anticipated residues of isocycloseram (ppm)
Tomatoes	Juice	0.362	0.2	0.072
	Paste		0.7	0.253
	Purée		0.3	0.109
	Dried tomatoes		3.8	1.376
Soybean	Refined oil	0.099	0.1	0.010
	Flour, soy milk		0.2	0.020
	Tofu		0.3	0.030
Almonds	Roasted	0.083	1.3	0.100
	Almond oil		5.0	0.415
Plums	Juice	0.229	<0.05	0.011

	Purée		0.2	0.046
	Dried prunes		3.2	0.733
Peach	Purée	0.270	<0.08	0.022
	Jam		<0.08	0.022
Apple	Juice	0.200	<0.06	0.012
	Sauce		<0.03	0.006
	Dried apples		0.05	0.010

Table 10 Food residue chemistry overview of metabolism studies and risk assessment

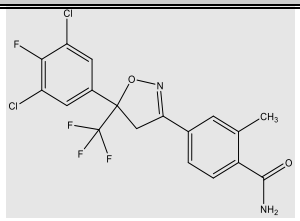
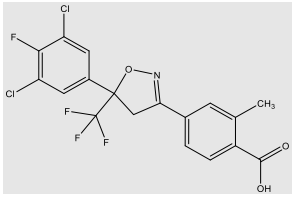
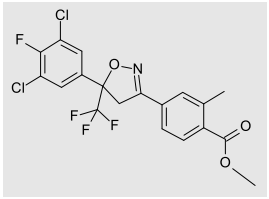
Plant studies	
Residue definition for enforcement and risk assessment **Primary crops (soybean, tomato, mustard green, paddy rice); Rotational crops (lettuce, radish, wheat)**	Isocycloseram
Metabolic profile in diverse crops	Similar in soybean, tomato, mustard green, and paddy rice for foliar uses
Animal studies	
Animals	**Ruminant and poultry**
Residue definition for enforcement and risk assessment	Isocycloseram
Metabolic profile in animals **(goat, hen, rat)**	Yes
Fat soluble residue	Yes

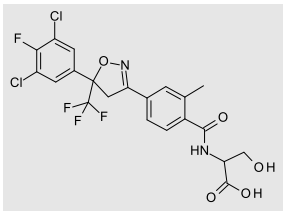
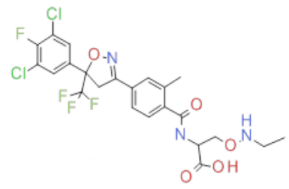
Dietary risk from food and drinking water					
Refined acute dietary exposure analysis, 95th percentile **ARfD = 0.012 mg/kg bw (all infants, children <12 years)** **ARfD = 0.13 mg/kg bw (males 13-49 years, adults 50-99 years)**	**Population**	**Estimated risk** **% of acute reference dose (ARfD)**			
		Food alone	**Food alone (excluding head lettuce)**	**Food and drinking water**	**Food (excluding head lettuce) and drinking water**
	All infants < 1 year	43.90	43.86	47.88	47.99
	Children 1–2 years	69.35	53.35	70.73	55.98
	Children 3–5 years	74.94	44.23	77.19	45.12

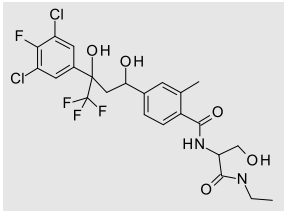
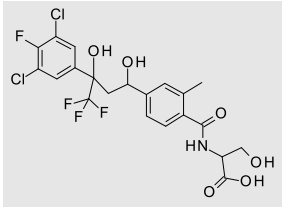
ARfD = 0.007 mg/kg bw (females 13-49 years) **Estimated acute drinking water concentration = 0.0057 ppm**	Children 6–12 years	54.98	30.60	55.85	32.02
	Males 13-49 years	4.86	2.26	4.20	2.35
	Adults 50-99 years	5.93	3.78	6.01	3.87
	Females 13-49 years	112.65	63.90	115.34	66.88
Refined chronic [non-cancer and cancer] dietary exposure analysis **ADI = 0.007 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.00094 ppm**	**Population**	**Estimated risk % of acceptable daily intake (ADI)**			
		Food alone	**Food alone (excluding head lettuce)**	**Food and drinking water**	**Food (excluding head lettuce) and drinking water**
	All infants < 1 year	10.9	10.8	11.9	11.9
	Children 1–2 years	21.3	21.2	21.7	21.6
	Children 3–5 years	15.7	15.5	16.0	15.8
	Children 6–12 years	9.7	9.5	9.9	9.7
	Youth 13–19 years	5.8	5.6	6.0	5.8
	Adults 20–49 years	7.5	7.3	7.8	7.5
	Adults 50-99 years	8.6	8.4	8.9	8.6
	Total population	8.7	8.4	8.9	8.7

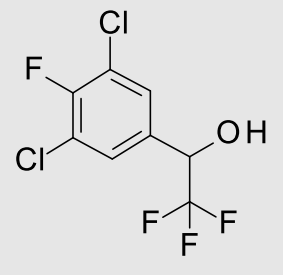
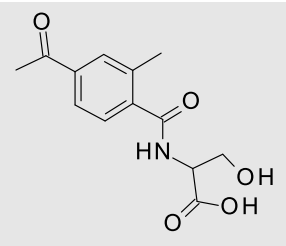
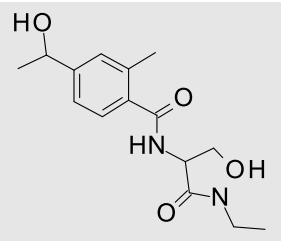
Table 11 Transformation products of isocycloseram in the environment

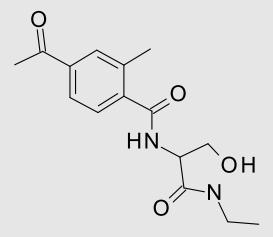
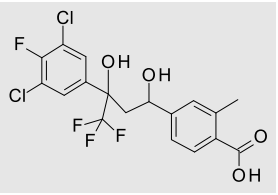
Code and chemical name	Chemical structure	Study		Max %AR (days)	%AR at study end (days)
SYN549431		Hydrolysis at 25°C and pH 7		< LOD	< LOD (29)
		Soil Photo-transformation	Dry Soil	6.5% (12)	6.4 (17)
			Moist Soil	6.1% (17)	≥ 6.1% (17)

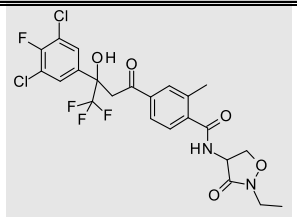
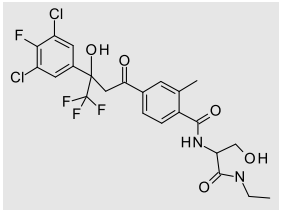
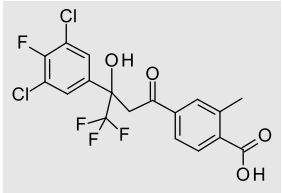
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
Molecular weight: 435.21 g/mol		Aqueous Phototransformation in pH 4 buffer	35% (15)	21.1% (20)
		Aerobic soil	5.3% (63)	4.6% (120)
		Anaerobic soil	6.2% (150)	6.2% (150)
		Aerobic aquatic with sediment	8.4% (148)	8.4% (148)
		Aerobic aquatic with sediment	< 5% (99)	< 5% (99)
		Anaerobic aquatic with sediment	< 5% (104)	< 5% (104)
		Field studies	4.6% (316)	2.9% (447-449)
		Koc	296500 (estimated)	
SYN549107 Synonym identifier in ecotox study: SYN547950 Molecular weight: 436.19 g/mol		Hydrolysis at 25°C and pH 7	< LOD	< LOD (29)
		Soil Phototransformation (Moist soil)	0.7% (17)	0.7% (17)
		Aqueous Phototransformation in Water with pH 4	3.1% (15)	<LOD (20)
		Aerobic soil	27.4% (120)	27.4% (120)
		Anaerobic soil	5.9% (31)	0.1% (150)
		Aerobic aquatic with sediment	11.3% (117)	11.3% (117)
		Aerobic aquatic with sediment	7.3% (99)	7.3% (99)
		Anaerobic aquatic with sediment	< LOD	< LOD (104)
		Field studies	3.4% (441)	2.9% (538)
		Koc	1139 – 9400 (empirical)	
SYN550738 Synonym identifier in ecotox study: SYN550918		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	10.9% (120)	10.9% (120)
		Anaerobic soil	Not Measured	Not Measured

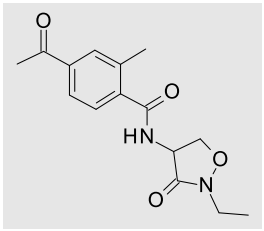
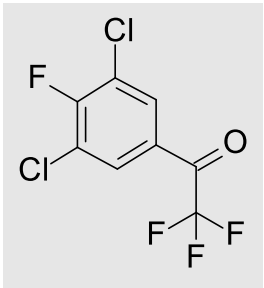
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
Molecular weight: 450.22 g/mol		Aerobic aquatic with sediment	< LOD	< LOD (99)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Anaerobic aquatic with sediment	< LOD	< LOD (104)
		Field studies	1.1% (441)	0.9% (538)
		Koc	105928 – 263662 (empirical)	
SYN549543 Molecular weight: 523.27 g/mol		Hydrolysis at 25°C and pH 7	pH 7: < LOD	pH 7: < LOD (29)
		Soil Phototransformation	< LOD	< LOD (20)
		Aqueous Phototransformation in Water with pH 4	Not Measured	Not Measured
		Aerobic soil	7.2% (7)	3.2% (120)
		Anaerobic soil	< 8.2% (90)	< 5.1% (150)
		Aerobic aquatic with sediment	6.2 (13)	2.1% (147)
		Aerobic aquatic with sediment	< 5% (99)	< 5% (99)
		Anaerobic aquatic with sediment	11.3% (8)	1.3% (104)
		Field studies	2.6% (58)	0.7% (449)
		Koc	6286 (estimated)	
SYN551203 Molecular weight: 566.34 g/mol		Hydrolysis at 25°C and pH 7	6.3% (25)	4.1% (29)
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	22.2% (75)	13.4% (150)
		Aerobic aquatic with sediment	< 5% (99)	< 5% (99)
		Aerobic aquatic with sediment	<5% (148)	<5% (148)
		Anaerobic aquatic with sediment	28.0% (8)	< LOD (104)
		Field studies	Not Measured	Not Measured

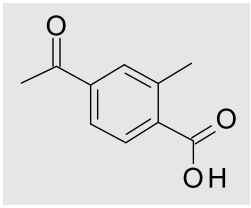
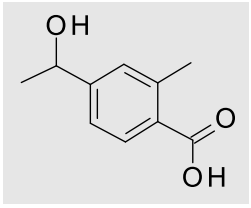
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Koc	484700 (estimated)	
SYN550455 Molecular weight: 555.36 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	19.2% (150)	19.2% (150)
		Aerobic aquatic with sediment	8.5% (14)	2.8% (99)
		Aerobic aquatic with sediment	33.5% (148)	33.5% (148)
		Anaerobic aquatic with sediment	12.6 (104)	12.6 (104)
		Field studies	< LOD	< LOD (538)
		Koc	3876 (estimated)	
SYN551248 Molecular weight: 528.29 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	11.6% (150)	11.6% (150)
		Aerobic aquatic with sediment	< LOD	< LOD (147)
		Aerobic aquatic with sediment	< LOD	< LOD (99)
		Anaerobic aquatic with sediment	< LOD	< LOD (104)
		Field studies	< LOD	< LOD (538)
		Koc	460 (estimated)	
SYN549546 Molecular weight: 263.02 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured

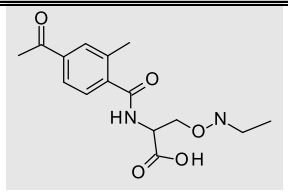
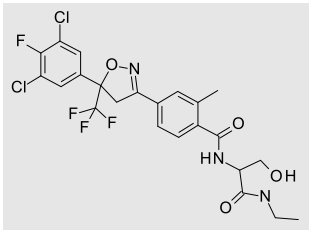
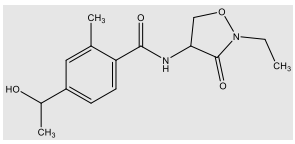
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	48.5% (150)	48.5% (150)
		Aerobic aquatic with sediment	30.5 (100)	24.2 (148)
		Aerobic aquatic with sediment	26.8% (60)	20.1% (99)
		Anaerobic aquatic with sediment	80.9 (63)	78.2 (105)
		Field studies	2.4 (441)	0.4% (449)
		Koc	617 (estimated)	
SYN551415 Molecular weight: 265.27 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	7.8% (60)	<LOD (150)
		Aerobic aquatic with sediment	< LOD (99)	< LOD (99)
		Aerobic aquatic with sediment	< LOD (148)	< LOD (148)
		Anaerobic aquatic with sediment	22.4 (12)	< LOD (105)
		Field studies	Not Measured	Not Measured
		Koc	39 (estimated)	
SYN550321 Molecular weight: 294.35 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	14.1% (122)	11.1% (150)
		Aerobic aquatic with sediment	< LOD	< LOD (148)
		Aerobic aquatic with sediment	< LOD	< LOD (99)

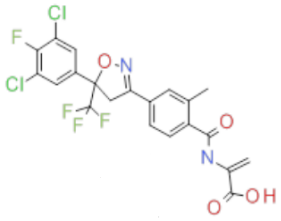
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Anaerobic aquatic with sediment	31.9% (104)	31.9% (104)
		Field studies	< LOD	< LOD (538)
		Koc	10 (estimated)	
SYN550603 Synonym identifier in ecotox study: SYN551513 Molecular weight: 292.34 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	11.1% (122)	6.8% (150)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Aerobic aquatic with sediment	12.6 (27)	2.1% (146)
		Anaerobic aquatic with sediment	26.6% (63)	24.3% (105)
		Field studies	< LOD	< LOD (538)
		Koc	10 (estimated)	
SYN551113 Molecular weight: 441.21 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	< 22.2% (75)	< 16.8% (150)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Aerobic aquatic with sediment	9.1% (146)	9.1% (146)
		Anaerobic aquatic with sediment	6.0% (104)	6.0% (104)
		Field studies	< LOD	< LOD (538)
		Koc	996.5 (estimated)	
SYN549433		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured

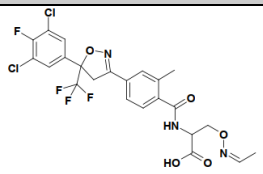
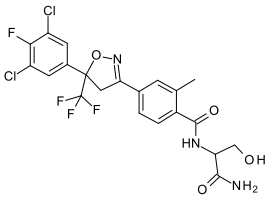
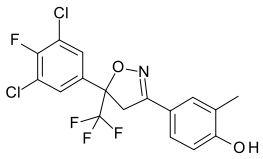
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
Molecular weight: 551.33 g/mol		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	< 18.2% (60)	< 13.4% (150)
		Aerobic aquatic with sediment	18.3% (8)	0.2% (148)
		Aerobic aquatic with sediment	11.4% (14)	1.5% (99)
		Anaerobic aquatic with sediment	16.9% (12)	< LOD (104)
		Field studies	0.6% (0)	< LOD (538)
		Koc	6242 (estimated)	
SYN550602 Synonyms identified for ecotox study: SYN551754 Molecular weight: 553.34 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	14.7 (90)	11.6% (150)
		Aerobic aquatic with sediment	30.3% (27)	17.0 (147)
		Aerobic aquatic with sediment	13.8% (14)	4.3% (99)
		Anaerobic aquatic with sediment	11.0% (27)	< LOD (105)
		Field studies	< LOD	< LOD (538)
		Koc	288 (estimated)	
SYN551190 Molecular weight: 439.19 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	6.2 % (150)	6.2 % (150)

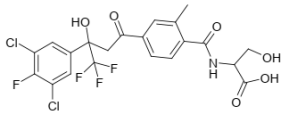
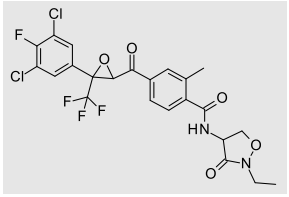
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Aerobic aquatic with sediment	10.8 % (61)	8.7 % (146)
		Aerobic aquatic with sediment	11.0% (99)	11.0% (99)
		Anaerobic aquatic with sediment	< 5%	< 5% (105)
		Field studies	Not Measured	Not Measured
		Koc	1539 (estimated)	
SYN549557 Molecular weight: 290.32 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	5.6 % (150)	5.6 % (150)
		Aerobic aquatic with sediment	< 5% (148)	< 5% (148)
		Aerobic aquatic with sediment	6.2% (14)	< LOD (99)
		Anaerobic aquatic with sediment	44.6% (8)	1.4% (105)
		Field studies	Not Measured	Not Measured
		Koc	39.1 (estimated)	
SYN548569 Molecular weight: 261.00 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	11.4 % (90)	< LOD (150)
		Aerobic aquatic with sediment	< 5% (148)	< 5% (148)
		Aerobic aquatic with sediment	2.0% (28)	< LOD (99)
		Anaerobic aquatic with sediment	44.9% (12)	0.5% (104)

Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Field studies	3.9% (28)	< LOD (538)
		Koc	954.3 (estimated)	
SYN549110 Molecular weight: 178.19 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	18.3% (122)	12.6% (150)
		Aerobic aquatic with sediment	< LOD	< LOD (148)
		Aerobic aquatic with sediment	< LOD	< LOD (99)
		Anaerobic aquatic with sediment	55.7% (41)	33.5% (105)
		Field studies	< LOD	< LOD (538)
		Koc	10 (estimated)	
SYN551057 Molecular weight: 180.21 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	17.8% (122)	13.6% (150)
		Aerobic aquatic with sediment	< LOD	< LOD (147)
		Aerobic aquatic with sediment	< LOD	< LOD (99)
		Anaerobic aquatic with sediment	< 16.3% (63)	< 7.2% (104)
		Field studies	< LOD	< LOD (538)
		Koc	10 (estimated)	
SYN551441		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured

Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
Molecular weight: 308.34 g/mol		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	Not Measured	Not Measured
		Aerobic aquatic with sediment	< LOD (99)	< LOD (99)
		Aerobic aquatic with sediment	< LOD (148)	< LOD (148)
		Anaerobic aquatic with sediment	11.7% (8)	< LOD (104)
		Field studies	Not Measured	Not Measured
		Koc	16.5 (estimated)	
SYN550737 Synonym: identified as SYN551753 in ecotox studies. Molecular weight: 550.30 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	< 5.0% (46)	< 5.0% (150)
		Aerobic aquatic with sediment	26.2% (5)	0.4% (147)
		Aerobic aquatic with sediment	11.1% (14)	3.9% (99)
		Anaerobic aquatic with sediment	< 5.0%	< 5.0% (105)
		Field studies	Not Measured	Not Measured
		Koc	100 000 (estimated)	
SYN549548 Molecular weight: 292.34 g/mol		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured

Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	Not Measured	Not Measured
		Aerobic aquatic with sediment	< LOD (148)	< LOD (148)
		Aerobic aquatic with sediment	< 5% (99)	< 5% (99)
		Anaerobic aquatic with sediment	10.3% (12)	< LOD (105)
		Field studies	Not Measured	Not Measured
		Koc	25.3 (estimated)	
Minor transformation products				
Code and chemical name	**Chemical structure**	**Study**	**Max %AR (days)**	**%AR at study end (days)**
SYN551485		Hydrolysis at 25°C and pH 7	pH 7: < LOD	pH 7: < LOD (29)
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in Water with pH 4	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	Not Measured	Not Measured
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Anaerobic aquatic with sediment	Not Measured	Not Measured
		Field studies	Not Measured	Not Measured
		Koc	68520 (estimated)	
SYN551478		Hydrolysis at 25°C and pH 7	< LOD	< LOD (29)
		Soil Phototransformation	< LOD	< LOD (17)

Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	Not Measured	Not Measured
		Aerobic aquatic with sediment	< LOD	< LOD (99)
		Aerobic aquatic with sediment	< LOD (148)	< LOD (148)
		Anaerobic aquatic with sediment	< LOD (104)	< LOD (104)
		Field studies	Not Measured	Not Measured
		Koc	791 100 (estimated)	
SYN549544		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in Water with pH 4	4.4% (10)	3.2% (20)
		Aerobic soil	4.0% (91)	3.5% (120)
		Anaerobic soil	Not Measured	Not Measured
		Aerobic aquatic with sediment	< LOD	< LOD (148)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Anaerobic aquatic with sediment	< LOD	< LOD (104)
		Field studies	Not Measured	Not Measured
		Koc	No data. (estimation not performed)	
SYN551030		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in Water with pH 4	Not Measured	Not Measured
		Aerobic soil	5.0% (91)	4.0% (120)

Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Anaerobic soil	Not Measured	Not Measured
		Aerobic aquatic with sediment	< LOD	< LOD (148)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Anaerobic aquatic with sediment	< LOD	< LOD (104)
		Field studies	Not Measured	Not Measured
		Koc	No data. (estimation not performed)	
SYN549554		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	< 5% (150)	< 5% (150)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Anaerobic aquatic with sediment	9.2% (12)	< LOD (104)
		Field studies	Not Measured	Not Measured
		Koc	No data. (estimation not performed)	
SYN551324		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	≥ 9.4% (150)	≥ 9.4% (150)
		Aerobic aquatic with sediment	Not Measured	Not Measured

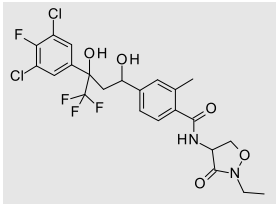
Code and chemical name	Chemical structure	Study	Max %AR (days)	%AR at study end (days)
		Aerobic aquatic with sediment	Not Measured	Not Measured
		Anaerobic aquatic with sediment	Not Measured	Not Measured
		Field studies	Not Measured	Not Measured
		Koc	20 190 (estimated)	
SYN549434		Hydrolysis	Not Measured	Not Measured
		Soil Phototransformation	Not Measured	Not Measured
		Aqueous Phototransformation in water with pH 4 buffer	Not Measured	Not Measured
		Aerobic soil	Not Measured	Not Measured
		Anaerobic soil	< 5.0% (150)	< 5.0% (150)
		Aerobic aquatic with sediment	< LOD (148)	< LOD (148)
		Aerobic aquatic with sediment	< 5.0% (99)	< 5.0% (99)
		Anaerobic aquatic with sediment	< 5.0%	< 5.0% (105)
		Field studies	Not Measured	Not Measured
		Koc	No data. (estimation not performed)	

Table 12 Estimated environmental concentration (EEC) for isocycloseram in the environment (excluding birds and small wild mammals) from outdoor foliar spray

Environmental compartment	EEC	Method of calculation	Notes
Terrestrial: screening level risk assessment			
Soil	0.02 mg a.i./kg soil	Calculated based on the maximum application of 50 g a.i./ha. The maximum single application rate is equal to the maximum cumulative application rate as a single application of 50 g a.i./ha is the highest proposed annual rate for turf. The representative half-life in aerobic soil was therefore not used in the calculation of the screening level soil EEC.	EECs in mg a.i./kg dw soil were used to evaluate risks to earthworms and other soil-dwelling invertebrates.

Environmental compartment	EEC		Method of calculation	Notes
			The EEC in soil was calculated based on the maximum cumulative application rate to soil, assuming a soil bulk density of 1.5 g/cm^3 and a soil depth of 15 cm.	
Foliar surfaces	On-field Turf	50 g a.i./ha	The maximum foliar application rate of 50 g a.i./ha. The maximum single application rate represents the maximum cumulative application rate as a single application of 50 g a.i./ha is the highest proposed annual rate.	EECs used to evaluate risks to non-target terrestrial plants (seedling emergence) and non-target foliar dwelling terrestrial invertebrates/beneficial arthropods. It is noted that multiple use scenarios were considered for beneficials at screening level because of the range of EECs based on drift and deposition/distribution factors.
	Off-field Turf	3.0 g a.i./ha	On-field screening EEC of 50 g a.i./ha multiplied by 6% drift (field sprayer application equipment, ASABE droplet size: Medium).	
	On-field Orchard	32.3 g a.i./ha	Calculated based on 2 applications of 20 g a.i./ha with 7-day intervals and a 10-day default half life.	
	Off-field Orchard	23.9 g a.i./ha	On-field screening EEC of 32.3 g a.i./ha multiplied by 74% drift (early season airblast spray equipment).	
	On-field other field crops	32.3 g a.i./ha	Calculated based on 2 applications of 20 g a.i./ha with 7-day intervals and a 10-day default half life.	
	Off-field other field crops	1.9 g a.i./ha	On-field screening EEC of 32.3 g a.i./ha multiplied by 6% drift.	
Adult bee contact acute	Turf	0.12 µg a.i./bee	AR_{Metric} · (2.4 µg a.i./bee)	AR = application rate in kg a.i./ha *Based on food consumption rates for larvae (0.124 g/day) and adult (0.292 g/day) worker bees and concentration in pollen and nectar. For larvae in terms of µg a.i./bee, when residues are measured in pollen and nectar, the consumption equation is as follows ((0*JellyMeasure+120*NectarMeasure+
Adult bee oral acute	Turf	1.43 µg a.i./bee/day	AR_{Metric} · (98 µg a.i./g) · (0.292 g/day)	
Adult bee diet chronic, bee larva diet acute and chronic	Turf	4.90 mg a.i./kg diet	AR_{Metric} · (0.098 mg a.i./g) ÷ (1 kg diet/ha)	

Environmental compartment	EEC		Method of calculation	Notes
				3.6*PollenMeasure)/ 1000000) For larvae in terms of mg a.i./kg diet the consumption equation is as follows: NectarMeasure*120/ (120+3.6) + PollenMeasure *3.6/(120+3.6))/100 0
Terrestrial: refined risk assessment				
Foliar surfaces (refined turf)	On-field	20 g a.i./ha	Calculated based on the maximum cumulative application rate of 50 g a.i./ha multiplied by a foliar deposition fraction of 40%.	EECs used to evaluate risks to foliar-dwelling beneficial arthropods and terrestrial plants.
	Off-field	0.30 g a.i./ha	Calculated based on the maximum cumulative application rate of 50 g a.i./ha multiplied by a spray drift deposition factor of 6% (field sprayer application equipment, ASABE droplet size: Medium) and a vegetation distribution factor of 10%.	
Foliar surface (refined orchard)	On-field	21.7 g a.i./ha	Calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval, the field measured DT_{50} of 4.7 days and a foliar deposition fraction of 80%.	
	Off-field	2.0 g a.i./ha	Calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval, the field measured DT_{50} of 4.7 days, a spray drift deposition factor of 74% (early season airblast spray equipment) and a vegetation distribution factor of 10%.	
Foliar surface (refined for other crops)	On-field	21.7 g a.i./ha	Calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval, the field measured DT_{50} of 4.7 days and a foliar deposition fraction of 80%.	
	Off-field	0.16 g a.i./ha	Calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval, the field measured DT_{50} of 4.7 days, a spray drift deposition factor of 6% (field sprayer application equipment, ASABE droplet size: Medium) and a vegetation distribution factor of 10%.	

Environmental compartment	EEC		Method of calculation	Notes
Water: screening level risk assessment (freshwater and marine)				
Water depth:	**15 cm**	**80 cm**	Calculated based on one single application of 50 g a.i./ha for turf and considering direct overspray to a 1 ha wetland with depths of 15 and 80 cm.	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms.
Water depth EEC	33.3 µg a.i./L	6.25 µg a.i./L		
Water: refined risk assessment - spray drift to freshwater and estuarine/marine environments - Turf				
Water depth:	**15 cm**	**80 cm**	Calculated based on the maximum cumulative application rate of 50 g a.i./ha multiplied by a spray drift deposition factor of 6% (Field sprayer application equipment, ASABE droplet size: Medium).	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms.
EEC	2.0 µg a.i./L	0.375 µg a.i./L		
Water: refined risk assessment - spray drift to freshwater environments – Orchard crops				
Water depth:	**15 cm**	**80 cm**	Calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval, the aerobic aquatic representative half-life of 198.9 days and a spray drift deposition factor of 74% (early season airblast spray equipment).	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms.
EEC	19.46 µg a.i./L	3.66 µg a.i./L		
Water: refined risk assessment - spray drift to estuarine/marine environments – Orchard crops				
Water depth:	**15 cm**	**80 cm**	Calculated based on 1 application of 30 g a.i./ha and a spray drift deposition factor of 74% (early season airblast spray equipment).	EECs in surface water at 80-cm depth used to evaluate risks to aquatic organisms.
Water depth EEC	N/A	2.78 µg a.i./L		
Water: refined risk assessment - spray drift to freshwater environments – other field crops				
Water depth:	**15 cm**	**80 cm**	Calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval, the aerobic aquatic representative half-life of 198.9 days and a spray drift deposition factor of 6% (Field sprayer application equipment, ASABE droplet size: Medium).	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all
Water depth EEC	1.6 µg a.i./L	0.30 µg a.i./L		

Environmental compartment	EEC			Method of calculation	Notes
					other aquatic organisms.
Water: refined risk assessment - spray drift to estuarine/marine environments – other field crops					
Water depth:	**15 cm**	**80 cm**		Calculated based on 1 application of 30 g a.i./ha and a spray drift deposition factor of 6% (Field sprayer application equipment, ASABE droplet size: Medium).	EECs in surface water at 80-cm depth used to evaluate risks to aquatic organisms.
Water depth EEC	N/A	0.23 µg a.i./L			
Water: refined risk assessment – runoff to freshwater and estuarine/marine environments - Turf					
Water depth:	**15 cm**	**80 cm**	**Pore water**	Calculated based on the maximum application of 50 g a.i./ha. The maximum single application rate is equal to the maximum cumulative application rate as a single application of 50 g a.i./ha is the highest proposed annual rate for turf. The representative half-life in aerobic water was therefore not used in the calculation of the screening level water EEC. For runoff, EECs in water are calculated by modelling a 10-ha field adjacent to 1-ha water bodies of two different depths, 80 cm and 15 cm.	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms. EECs in pore water were used to evaluate risk to sediment dwelling organisms.
24 hours	0.24 µg a.i./L	0.099 µg a.i./L	N/A		
96 hours	0.081 µg a.i./L	0.063 µg a.i./L	N/A		
21 days	N/A	0.027 µg a.i./L	0.005 µg a.i./L		
60 days	0.014 µg a.i./L	0.014 µg a.i./L	N/A		
Water: refined risk assessment - runoff – Orchard crops					
Water depth:	**15 cm**	**80 cm**	**Pore water**	Modelled based on the maximum cumulative application rate in water of 39.518 g a.i./ha which was calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval and the aerobic aquatic representative half-life of 198.9 days.	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms. EECs in pore water were used to evaluate risk to sediment dwelling organisms.
24 hours	N/A	0.106 µg a.i./L	N/A		
96 hours	0.069	0.066 µg a.i./L	N/A		
21 days	N/A	0.023 µg a.i./L	0.004 µg a.i./L		
60 days	0.012 µg a.i./L	0.012 µg a.i./L	N/A		
Water: refined risk assessment - runoff – field crops other than orchard crops					
Water depth:	**15 cm**	**80 cm**	**Pore water**	Modelled based on the maximum cumulative application rate in water of 39.518 g a.i./ha which was calculated based on 2 applications of 20 g a.i./ha with a 7-day reapplication interval and	EECs in surface water at 15-cm depth were used to evaluate risk to amphibians, and the
24 hours	0.507 µg a.i./L	0.268 µg a.i./L	N/A		

Environmental compartment	EEC			Method of calculation	Notes
96 hours	0.208 µg a.i./L	0.204 µg a.i./L	N/A	the aerobic aquatic representative half-life of 198.9 days.	80-cm depth EECs were used to evaluate risks to all other aquatic organisms. EECs in pore water were used to evaluate risk to sediment dwelling organisms.
21 days	N/A	0.125 µg a.i./L	0.046 µg a.i./L		
60 days	0.057 µg a.i./L	0.063 µg a.i./L	N/A		

Table 13 Estimated environmental exposure for isocycloseram in the environment for birds and small wild mammals from foliar application

Environmental matrix	Application rate used to calculate the estimated environmental exposure (g a.i./ha)	Half-life used to calculate the maximum cumulative rate (days)	Estimated environmental exposure (EDE)[1]	Notes	Method of calculation
Diet of small-sized birds: insects (BW = 20 g)	Maximum foliage cumulative: 50	Default value: 10	EDE: 4.1 mg a.i./kg bw/day	FIR = 5.1 g dw diet/day	The EDE is calculated using the following formula: (FIR/BW) × EEC. BW = Body weight, FIR = Food ingestion rate. For birds with body weight less than or equal to 200 g: FIR (g dry weight/day) = 0.398(BW in g)$^{0.850}$.
Diet of medium-sized birds: insects (BW = 100 g)	Maximum foliage cumulative: 50	Default value: 10	EDE: 3.2 mg a.i./kg bw/day	FIR = 19.9 g dw diet/day	
Diet of large-sized birds: short grass (BW = 1000 g)	Maximum foliage cumulative: 50	Default value: 10	EDE: 2.1 mg a.i./kg bw/day	FIR = 58.1 g dw diet/day	
Diet of small-sized small wild mammals: insects (BW = 15 g)	Maximum foliage cumulative: 50	Default value: 10	EDE: 2.3 mg a.i./kg bw/day	FIR = 2.2 g dw diet/day	

Environmental matrix	Application rate used to calculate the estimated environmental exposure (g a.i./ha)	Half-life used to calculate the maximum cumulative rate (days)	Estimated environmental exposure (EDE)[1]	Notes	Method of calculation
Diet of medium-sized small wild mammals: short grass (BW = 35 g)	Maximum foliage cumulative: 50	Default value: 10	EDE: 4.5 mg a.i./kg bw/day	FIR = 4.5 g dw diet/day	For birds with body weight greater than 200 g: FIR (g dry weight/day) = $0.648(\text{BW in g})^{0.651}$. For small wild mammals: FIR (g dry weight/day) = $0.235(\text{BW in g})^{0.822}$ 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. The EECs for birds and mammals were calculated based on a single application of 50 g a.i./ha.
Diet of large-sized small wild mammals: short grass (BW = 1000 g)	Maximum foliage cumulative: 50	Default value: 10	EDE: 2.4 mg a.i./kg bw/day	FIR = 68.7 g dw diet/day	

EDE = Estimated Daily Exposure (mg a.i./kg bw/day) for birds and small wild mammals, specialized feeding guilds are considered for each category of animal weight to help determine exposure (herbivore, frugivore, insectivore and granivore).

Table 14 Estimated environmental concentration (EEC) for isocycloseram in the environment (excluding birds and small wild mammals) from in-furrow application

Environmental compartment	EEC		Method of calculation	Notes
Terrestrial: screening level risk assessment				
Soil	0.067 mg a.i./kg dw soil		The EEC in soil was calculated based on the maximum application rate of 150 g a.i./ha., assuming a soil bulk density of 1.5 g/cm^3 and a soil depth of 15 cm.	EECs in mg/kg dry weight soil were used to evaluate risks to earthworms and soil-dwelling beneficial arthropods.
Plant surfaces	On-field	Negligible	N/A	Used to evaluate on-field and off-field risks to beneficial arthropods and non-target terrestrial plants (vegetative vigour).
	Off-field	Negligible		
Bee matrices				
Bees (Contact and pollen and nectar)	(adult)	Negligible	Residues from in-furrow applications are not expected to translocate into pollen and/or nectar.	Used to evaluate risks to bees.
	(larvae)	Negligible		
	(adult, contact)	Negligible		
Water: screening level risk assessment				
Water depth:	**15 cm**	**80 cm**	EECs calculated based on one single application of 150 g a.i./ha. EECs in surface water were calculated considering a direct overspray of the maximum cumulative application rate to a 1 ha wetland with depths of 15 and 80 cm.	EECs in surface water at 15-cm depth were used to determine risk to amphibians, and the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms.
Water EECs	100 µg a.i./L	18.75 µg a.i./L		
Water: refined risk assessment – runoff to freshwater and estuarine/marine environments				
Water depth:	**15 cm**	**80 cm** / **Pore water**	EECs modelled based on one application of 150 g a.i./ha.	EECs in surface water at 15-cm depth were used to determine risk to amphibians, and the
24 hours	N/A	0.171 µg a.i./L / N/A		

Environmental compartment	EEC			Method of calculation	Notes
96 hours	0.170 µg a.i./L	0.140 µg a.i./L	N/A		80-cm depth EECs were used to evaluate risks to all other aquatic organisms. Pore water was used to evaluate risks to sediment dwelling organisms.
21 days	N/A	0.081 µg a.i./L	0.027 µg a.i./L		
60 days	N/A	0.042 µg a.i./L	N/A		

Table 15 Estimated environmental concentration (EEC) for isocycloseram in the environment (excluding birds and small wild mammals) from greenhouse foliar spray

Environmental compartment	EEC		Method of calculation	Notes
Terrestrial: screening level risk assessment				
Foliar surfaces	On-field greenhouse	168.584 g a.i./ha	Calculated based on the maximum proposed single application rate is 150.3 g a.i./ha and maximum proposed cumulative application rate is 180 g a.i./ha, a 7-day reapplication interval and the default foliar half-life of 10 days.	EECs used to evaluate risks non-target foliar dwelling terrestrial invertebrates and beneficial arthropods.
Adult bee contact acute	On-field greenhouse	0.361 µg a.i./bee	AR_{Metric} · (2.4 µg a.i./bee)	AR = application rate in kg a.i./ha *Based on food consumption rates for larvae (0.124 g/day) and adult (0.292 g/day) worker bees and concentration in pollen and nectar.
Adult bee oral acute	On-field greenhouse	4.301 µg a.i./bee/day	AR_{Metric} · (98 µg a.i /g) · (0.292 g/day)	
Adult bee and larva diet (acute and chronic)	On-field greenhouse	14.729 mg a.i./kg diet	AR_{Metric} · (0.098 mg a.i./g) ÷ (1 kg diet/ha)	
Terrestrial: refined risk assessment				
Foliar surfaces (greenhouse ornamentals)	On-field	128.7 g a.i./ha	Calculated based on the maximum proposed single application rate is 150.3 g a.i./ha and maximum proposed cumulative application	On and off-field EECs were calculated and compared with refined extended

Environmental compartment	EEC		Method of calculation	Notes
			rate is 180 g a.i./ha, a 7-day reapplication interval, the field-measured foliar DT_{50} of 4.7 days and a foliar deposition fraction of 80%.	laboratory endpoints.

Table 16 Toxicity to non-target terrestrial species

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
Invertebrates					
Earthworm (*Eisenia fetida*)	Isocycloseram Technical Purity: 96.9% w/w	14 days	14-d LC_{50}: >969 mg a.i./kg dw soil 0% mortality was observed up to the highest concentration tested.	N/A	3246216
	Isocycloseram Technical Purity: 98.4% w/w	56 days, reproduction	28-d LC_{50}: > 10 mg a.i./kg dw soil 56-d $NOEC_{repro}$: 10 mg a.i./kg dw soil	N/A	3246217
Honey bee (*Apis mellifera*)	Isocycloseram Technical Purity: 96.9% w/w – 98.8% w/w	96-hour contact adult	96-h LD_{50}: 0.26 µg a.i./bee	Highly toxic	3246199
		72-hour oral adult	48-h LD_{50}: 0.29 µg a.i./bee 72-h LD_{50}: 0.29 µg a.i./bee	Highly toxic	
		10-day diet adult	10-d $NOEDD_{mortality}$: 0.0028 µg a.i./bee/day (0.11 mg a.i./kg diet)	N/A	3246197
		72-hour larvae	72-h LD_{50}: 0.08 µg a.i./larva (3.88 mg a.i./kg diet)	Highly toxic	3246207
		22-day larvae (4-days exposure)	22-d $NOEDD_{emergence}$: 0.004 µg a.i./larva/day (0.1 mg a.i./kg diet)	N/A	3246206

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
		63-day colony feeding study (9 days exposure, 54 days post exposure observation period)	63-d NOEC: 0.28 mg a.i./kg diet	N/A	3246208
	SYN549106 (transformation product of isocycloseram) Synonym identifier in fate studies: SYN549431	96-hour contact adult	96-h LD_{50}: 0.072 µg a.i./bee	Highly toxic	3246200
		96-hour oral adult	96-h LD_{50}: 0.18 µg a.i./bee	Highly toxic	
Bumblebee *(Bombus terrestris L.)*	Isocycloseram Technical Purity: 96.9% w/w	48-hour oral adult	LD_{50}: 0.26 µg a.i./bee	Highly Toxic	3246198
		48-hour contact adult	LD_{50}: >11.9 µg a.i./bee	Practically nontoxic	
Parasitoid wasp (*Aphidius rhopalosiphi*)	SYN547407 DC 100 (Formulated product) Purity: 9.29% w/w	13-day glass plate 48-hours exposure (11 days observation)	48-h LR_{50}: 0.42 g a.i./ha 13-d $ER_{50\ reproduction}$: > 0.3 and < 0.6 g a.i./ha A 13-day $ER_{50\ reproduction}$ could not be determined due to high adult mortality in the test vessels above 0.3 g a.i./ha.		
	A21708E (Formulated product) Purity: 9.06% w/w	13-day extended lab applied to plant foliage	48-h LR_{50}: 2.46 g a.i./ha 13-d $ER_{50\ reproduction}$: > 2.44 A 13-day $ER_{50\ reproduction}$ could not be determined due to high adult mortality in the test vessels above 2.44 g a.i./ha.	N/A	3633674
Predatory mite (*Typhlodromus pyri*)	SYN547407 DC 100 (Formulated product) Purity: 9.29% w/w	14-day glass plate	7-d LR_{50}: 0.0059 g a.i./ha 14-d $ER_{50\ reproduction}$: 0.0041 g a.i./ha	N/A	3246210

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
	A21708E (Formulated product) Purity: 9.06% w/w	14-day extended lab (dried residues on foliage)	7-d LR_{50}: 0.0072 g a.i./ha 14-d $ER_{50\ reproduction}$: 0.006 g a.i./ha	N/A	3633672
Predatory mite (*Hypoaspis aculeifer*)	Isocycloseram Technical Purity: 98.4% w/w	14-day artificial soil substrate	14-d LC_{50}: 0.821 mg a.i./kg soil dw 14-d $EC_{50reproduction}$: 0.343 mg a.i./kg soil dw 14-d $NOEC_{reproduction}$: 0.171 mg a.i./kg soil dw	N/A	3246211
	SYN547950 (transformation product of isocycloseram)	14-day artificial soil substrate	14-d LC_{50}: 25 mg a.i./kg soil dw 14-d $EC_{50reproduction}$: 20.8 mg a.i./kg soil dw 14-d $NOEC_{reproduction}$: 5.8 mg/kg soil dw	N/A	3246212
	SYN549433 (transformation product of isocycloseram)	14-day artificial soil substrate	14-d LC_{50}: > 61.2 mg a.i./kg soil dw 14-d $EC_{50reproduction}$: > 61.2 mg a.i./kg soil dw (0% mortality observed at the highest test concentration of 61.2 mg a.i./kg soil dw) (7.1% reduction in reproduction (mean number of juveniles) at the highest test concentration of 61.2 mg a.i./kg soil dw) 14-d $NOEC_{reproduction}$: 34.0 mg/kg soil dw	N/A	3246213

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
	SYN550918 (transformation product of isocycloseram)	14-day artificial soil substrate	14-d LC_{50}: > 61.2 mg a.i./kg soil dw 14-d $EC_{50reproduction}$: > 61.2 mg a.i./kg soil dw (10% mortality observed at the highest test concentration of 61.2 mg a.i./kg soil dw) (39.8% reduction in reproduction (mean number of juveniles) at the highest test concentration of 61.2 mg a.i./kg soil dw) 14-d $NOEC_{reproduction}$: 10.5 mg/kg soil dw	N/A	3246214
Collembolan (*Folsomia candida*)	Isocycloseram Technical Purity: 98.4% w/w	28-day artificial soil substrate	28-d $EC_{50reproduction}$: 0.217 mg a.i./kg soil dw 28-d $NOEC_{reproduction}$: 0.095 mg a.i./kg soil dw	N/A	3246215
Birds					
Northern bobwhite quail *(Colinus virginianus)*	Isocycloseram Technical Purity: 96.9%	Single dose oral	LD_{50}: > 2000 mg a.i./kg bw No mortality was observed up to the highest dose tested.	Practically nontoxic	3246128
		5-day dietary	5-d LD_{50}: > 953 mg a.i./kg bw/day No mortality was observed at the highest dose tested.	Slightly toxic	3246131

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
		27-week reproduction	27-week $NOED_{reproduction}$: 25.3 mg a.i./kg bw/day 27-week $LOED_{reproduction}$: 83.4 mg a.i./kg bw/day Reproductive endpoints affected at the LOED: ↑ 27.9 % in cracked eggs ↓ 30.4 % in eggs set ↓ 28.9 % viable embryos ↓ 29.5 % live embryos ↓ 28.9 % number of hatchlings ↓ 30.6 % 14-day hatchling survival ↓ 26.7% eggs laid per hen	N/A	3246133
Mallard duck (*Anas platyrhynchos*)	Isocycloseram Technical Purity: 96.9%	Single dose oral	LD_{50}: > 2000 mg a.i./kg bw No mortality was observed up to the highest dose tested.	Practically nontoxic	3246130
		5-day dietary	5-day LD_{50}: 466.4 mg a.i./kg bw/day	Moderately toxic	3246132

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
		21-week reproduction	21-week $NOED_{reproduction}$: 14.6 mg a.i./kg bw/day 21-week $LOED_{reproduction}$: 52.5 mg a.i./kg bw/day Reproductive endpoints affected at the LOED: ↓ 5% in hatchling survival per number of hatchlings ↓ 3% in eggshell thickness ↓ 10% in 14-day offspring survivor weight	N/A	3246134
Canary (*Serinus canaria*)	Isocycloseram Technical Purity: 96.9%)	Single dose oral	LD_{50}: > 1500 mg a.i./kg bw No mortality was observed up to the highest dose tested.	Slightly toxic	3246129
Small wild mammals					
Wistar rat (*Rattus norvegicus*)	Isocycloseram Technical Purity: 96.9%)	Single dose oral (gavage)	LD_{50}: > 5000 mg a.i./kg bw No mortality was observed up to the highest dose tested.	Practically nontoxic	3245989
		2-generation reproduction (diet)	NOEL = 3.5 mg a.i./kg bw/day[2] LOEL = 10.4 mg a.i./kg bw/day[2] (Highest daily dose tested) Observed effects: F1 offspring: ↓ 9% of mean live birth index F1 offspring: ↓ 11% mean cumulative survival	N/A	3246019

Organism	Test substance	Exposure	Endpoint value	Effects/ Degree of toxicity[1]	PMRA No.
Vascular plants					
Four monocot species: onion, oat, ryegrass and maize.	SYN547407 SC (Formulated product)	Seedling emergence Single pre-emergence application	ER_{25}: 818 g a.i./ha (Lowest ER_{25} of all species tested) A maximum reduction of 25% mean foliar dry weight for sugar beet across all test species at the highest concentration tested.	N/A	3246143
Six dicot species: lettuce, oilseed rape, soybean, sugar beet, cucumber and tomato					
Four monocot species: onion, oat, ryegrass and maize.	SYN547407 SC (Formulated product)	Vegetative vigour Single post-emergence application at BBCH growth stages: 12 – 14.	ER_{25}: > 818 g a.i./ha (for all species tested) A maximum of 13% reduction in mean foliar dry weight was observed across all test species at the highest concentration tested.	N/A	3246144
Six dicot species: lettuce, oilseed rape, soybean, sugar beet, cucumber and tomato					

[1] USEPA classification (1985), where applicable.
[2] Corrected for isomer toxicity
N/A = not available

Table 17 Effects on bees during semi-field tunnel studies of isocycloseram applied during active bee foraging and flight

Study design	Results and overall conclusions	PMRA No.
Test species: Africanized honey bees (*Apis mellifera*) Test Substance: A20792A 050SC Formulated Product (5% w/w isocycloseram) Application rates: Test Group 1: Single application at 29.2 g a.i./ha Test Group 2: Single application at 48.8 g a.i./ha	There were limited effects observed on mortality and brood development for Africanized honey bees exposed to isocycloseram at single applications of either 29.2 or 48.8 g a.i./ha. Some mortality was observed in the positive control group, but to a lesser extent than expected. Based on the observed effects in the positive control, and	3246146

Study design	Results and overall conclusions	PMRA No.
Reference chemical rate: 400 g dimethoate/ha Crop: Soybean (*Glycine max*) Attractiveness: Low to moderate Exposure and observation Length: Colonies were exposed in tunnels for 8 days and observed for additional 21 days. Replicates: 3 tunnels per treatment group with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate.	the exposure crop in this study (soybean) which is not very attractive to bees, there was likely low exposure to isocycloseram in this study. There was also low foraging in all tents, including the control. This study would likely represent exposure to this crop (soybean), but it does not represent potential exposure to more attractive crops on the proposed label.	
Test species: Africanized honey bees (*Apis mellifera*) Test Substance: A21550L 400SC Formulated Product (34.8% w/w isocycloseram) Application rate: Three applications at 40.0 g a.i./ha on a 5-day re-application interval. Reference chemical rate: 400 g dimethoate/ha Crop: Cotton (*Gossypium hirsutum*) Attractiveness: Attractive. Application type and timing: First application: Foliar spray during full flowering one day before the hives were placed in the tunnels. Second and third applications: Foliar spray during full flowering during active bee foraging and flight. Exposure and observation length: Colonies were exposed in tunnels for 14 days with an additional 36 day observation period.	Hive strength and total brood decreased in all the test hives, including control groups, which suggests that the study was performed under unfavorable hive conditions (including decreased pollen supply). After the colonies were moved to the monitoring site colonies in all treatment groups decreased gradually in size until the final colony assessment. Overall, there was no statistical difference in adult or brood mortality or flight intensity between the control and isocycloseram treatment groups over the course of the study. Owing to study design issues, brood effects could not reliably be determined. Residue analysis results: Residues were measured in leaves, flowers, nectar, and pollen. Peak measured residues in leaves, flowers, nectar, and pollen	3246147

Study design	Results and overall conclusions	PMRA No.
Replicates: 4 tunnels per treatment group with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate. Residue collection: Yes.	were 13900, 975, 833 and 414 µg a.i./kg, respectively. 10-day mean measured residues in leaves and flowers and 8-day mean measured residues in nectar and pollen were 8596, 640.6, 108.5 and 38.0 µg a.i./kg, respectively.	
Test species: Honey bees (*Apis mellifera*) Test Substance: A21550L 400SC Formulated Product (34.8% w/w isocycloseram) Application rate: Single application of 82.0 g a.i./ha. Reference chemical: Dimethoate (trade name not specified). Crop: Cotton (*Gossypium hirsutum*) Attractiveness: Attractive. Exposure and observation length: Colonies were exposed in tunnels for 7 days, and additional 42 day observation period. Replicates: 4 tunnels per treatment with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate. Residue collection: Yes	No effects on adult mortality or foraging were observed under the study conditions. However, statistically-significant brood effects were observed seven days after the application of isocycloseram in the treatment groups and dimethoate toxic reference groups when compared to the control groups. Based on the results from this study, exposure to isocycloseram may pose a risk to honey bee colonies when applied to cotton (*Gossypium hirsutum*) at a rate of 82.0 g a.i./ha during active bee foraging and flight. Residue analysis results: Residues were measured in leaves, flowers, nectar, and pollen. Peak measured residues in leaves, flowers, nectar, and pollen were 10408, 942, 237 and 103 µg a.i./kg, respectively. 7-day mean measured residues in leaves and flowers and 8-day mean measured residues in nectar and pollen were 5260, 575, 137.7 and 36.9 µg a.i./kg, respectively.	3246148
Test species: Honey bees (*Apis mellifera*) Test Substance: A21377X SC 200 Formulated Product (18.5% isocycloseram)	Overall, there were no significant differences in foraging activity, colony strength or brood cells between the control, test item or	3246154

Study design	Results and overall conclusions	PMRA No.
Application rates: Application 1: 40.0 g a.i./ha Application 2: Applied 10 days after application 1 at a rate of 40.0 g a.i./ha Application 3: Applied 7 days after application 2 at a rate of 69.9 g a.i./ha. Reference chemical rate: 600 g dimethoate/ha Crop: Soybean (Glycine max) Attractiveness: Low to moderate Application type and timing: First application: Foliar spray during full flowering before bees were introduced. Second and third applications occurred during bloom and during bee flight. Exposure and observation length: Colonies were exposed in tunnels for 10 days with an additional 39 days of observation. Replicates: 4 tunnels per treatment with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate. Residue collection: Yes.	toxic reference. Heavy rainfall may have had a significant impact on exposure which is further confirmed by the lack of effects in the positive reference group. As such, the results of this study are not reliable for use in a risk assessment. Residue analysis results: Residues were measured in leaves, flowers, anthers, and nectar from foraging bees. Peak measured residues in leaves, flowers, anthers, and nectar were 17000, 1120, 1780 and 25.5 µg a.i./kg, respectively. 12-day mean measured residues in leaves, flowers, anthers and nectar from foraging bees were 7707, 632, 574 and 11.7 µg a.i./kg, respectively.	
Test species: Honey bees (*Apis mellifera*) Test Substance: A21708F 100DC Formulated Product (9.25% isocycloseram) Application rates: Test group 1: Single application of 60 g a.i./ha Test group 2: Single application of 90 g a.i./ha Test group 3: Single application of 120 g a.i./ha. Reference chemical: Agritoato 400 containing dimethoate.	The validity criteria for the field phase of this study was not met. The protocol states that the brood termination rate cannot exceed 40% for the untreated control group. Due to extenuating circumstances with weather conditions, the control group termination rate was greater than 40%. As such the study was terminated.	3246152

Study design	Results and overall conclusions	PMRA No.
Crop: Buckwheat (*Fagopyrum esculentum*) Attractiveness: High Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate. Residue collection: Yes.	The effects of the test substance on honey bees were not investigated. <u>Residue analysis results:</u> A review was not conducted because the study was terminated. Environmental conditions: Not applicable as study was terminated. Confirmation of exposure: Not applicable as study was terminated.	

Table 18 Effects on bees during semi-field tunnel studies of isocycloseram applied either before or after active bee foraging and flight

Study design	Results and overall conclusions	PMRA No.
Test species: Africanized Honey bees (*Apis mellifera*) Test Substance: A21550L 400SC Formulated Product (34.8% w/w isocycloseram) Application rates: Group 1: Application 1: 41.6 g a.i./ha Application 2: 89.5 g a.i./ha Application 3: 89.5 g a.i./ha Group 2: Application 1: 39.9 g a.i./ha Application 2: 90.6 g a.i./ha Application 3: 88.1 g a.i./ha Reference chemical rate: 400 g dimethoate/ha	Group 1: Statistically significant effects on mortality were observed 5 days after the second application (89.5 g a.i./ha). However, this mortality is considered low, and was only recorded on one day and is well within the range of observed mortality on several other days in the negative control group. As well, it is much lower than the positive control (103.8 dead bees). It is expected that this low transient mortality is unlikely to cause lasting brood or colony effects as is shown in the brood data where no statistical differences in the number of brood cells (eggs, larvae and pupae) were observed between treatment group 1 when compared to the negative	3246149

Study design	Results and overall conclusions	PMRA No.
Crop: Niger, (*Guizotia abyssinica*) Attractiveness: High Application type and timing: Group 1: Applications: First foliar spray during full flowering applied 1 day before bee colonies were placed in the exposure tunnels. Applications 2 and 3 were made in the evening, 5 days apart. Group 2: Applications: First foliar spray during full flowering applied 1 day before bee colonies were placed in the exposure tunnels. Second application was made 5 days later in evening and third application was made 5 days later in morning. Exposure and observation length: Colonies were exposed in tunnels for 10 days with an additional 39 days observation period. Replicates: 4 tunnels per treatment with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate. Residue collection: Yes.	control. Overall, this would not be considered an effect in the study. No statistically-significant effects were observed on foraging activity, behavior abnormalities, brood development, and brood termination rate. Group 2: Statistically-significant effects on mortality were observed 0 and 4 days after the second application (90.6 g a.i./ha). Although statistically higher, the mortality is considered low, was only recorded on 2 days in the study and is well within the range of observed mortality on several other days in the negative control group. As well, it is much lower than the positive control. It is expected that this low transient mortality is unlikely to cause lasting brood or colony effects as is shown in the brood data where no statistical differences in the number of brood cells (eggs, larvae and pupae) were observed between treatment group 2 when compared to the negative control. A significant yet transient reduction in foraging activity compared to negative controls was observed 0 days after the third treatment. Residue analysis results: Group 1: Peak measured residues in leaves, flowers, nectar from foraging bees, pollen from foraging bees and pollen from pollen traps were 26 300, 9680, 44.4, 5200 and 2480 µg a.i./kg, respectively. 10-day mean measured residues in leaves, flowers, nectar from foraging bees, pollen	

Study design	Results and overall conclusions	PMRA No.
	from foraging bees and pollen from pollen traps were 17490, 5307, 13, 2407 and 767 µg a.i./kg, respectively. Group 2: Peak measured residues in leaves, flowers, nectar from foraging bees, pollen from foraging bees and pollen from pollen traps were 37 200, 10 600, 41.1, 3200 and 1060 µg a.i./kg, respectively. 10-day mean measured residues in leaves, flowers, nectar from foraging bees, pollen from foraging bees and pollen from pollen traps were 19 200, 6075, 11.7, 1507 and 454 µg a.i. /kg, respectively.	
Test species: Honey bees (*Apis mellifera*) Test Substance: A21708F 100DC Formulated product (9.25% isocycloseram) Application rate: Group 1: Single Application of 60.1 g a.i./ha Group 2: Single Application of 120.5 g a.i./ha Reference chemical rate: 479.3 g dimethoate/ha Crop: buckwheat (*Fagopyrum esculentum*) Attractiveness: High Application type and timing: Foliar spray during full flowering at nightfall after active foraging and bee flight. Exposure and observation length: Colonies were exposed in tunnels for 6 days with an additional 5 days of observation period. Replicates: 4 tunnels per treatment with 1 colony per tunnel.	No statistically significant differences were detected between the negative control and isocycloseram treatment groups for any of the measurement endpoints evaluated. However, for treatment group 2 (120.5 g a.i./ha), seven days after treatment, mortality increased. Six days after treatment, mortality was 58 dead bees which increased to 110 dead bees 7 days after treatment. Mean mortality 7 days after treatment (110 dead bees) was approximately 350% higher than the mean mortality of the control (25 dead bees), and similar to mortality in the positive control (147 dead bees). There was a general trend of higher mortality in the treatment hives compared to control hives. Therefore, there were negligible effects at an application of 60.1 g a.i./ha, and potential effects at 120.5 g a.i./ha. The assessment on 7 DAE prompted a removal of the hives in the early morning of 8 DAE based on the lack	3246150

Study design	Results and overall conclusions	PMRA No.
Observed bee/colony health parameters: mortality, foraging activity, behavior abnormalities, brood development, and brood termination rate.	of pollen in the untreated control tunnels. All four hives had less than 50% total pollen stores, with one colony having only 5%. Some of the treated colonies still had pollen and honey stores available.	
Test species: Honey bees (*Apis mellifera*) Test Substance: A21708F 100DC Formulated Product (9.27% w/w isocycloseram) Application rates: Trial 1: Group 1: 75.5 g a.i./ha Group 2: 111.3 g a.i./ha Group 3: 147.9 g a.i./ha Trial 2: Group 1: 59.62 g a.i./ha Reference chemical rate: Trial 1: 423.7 g dimethoate/ha Trial 2: 433.9 g dimethoate/ha Crop: buckwheat (*Fagopyrum esculentum*) Attractiveness: High Application type and timing: Trial 1 and 2: Foliar spray during full flowering applied 3 days after the hives were placed in the tunnels at nightfall after active foraging and bee flight. Exposure and observation length: Colonies were exposed in tunnels for 7 days, with an additional 59 days of observation. Replicates: 4 tunnels per treatment with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior	Trial 1: No statistically-significant differences between test groups and the negative control group were reported by the study authors for mortality; however, the 7-day cumulative adult mortality represents an increase of 376, 445, 566 and 869% in mortality for the 75.5, 111.3, 147.9 g a.i./ha and positive control (dimethoate) test groups, respectively. As such, there is potential transient effects to adults. There was no dose related effects to brood. Trial 2: It is noted by the study author that in Trial 2, the brood termination rate for eggs was 100% for the Control, T1 and Reference groups. Poor weather during confinement inhibited the foraging ability of all colonies, rendering a high brood mortality that was not due to any exposure effect. As such, evaluation of brood effects is not reliable. No statistically significant differences in adult mortality were observed in the 59.62 g a.i./ha treatment group when compared to the control. Residue analysis results:	3246151

Study design	Results and overall conclusions	PMRA No.
abnormalities, brood development, and brood termination rate. Residue collection: Yes.	Residues were measured in leaves, flowers, nectar from foraging bees, nectar from hives and pollen from foraging bees. Residues from hive nectar were only collected after 37 DAT and 65 DAT and were not considered representative of the 7-day exposure period. Trial 1: Group 1: Peak measured residues in leaves, nectar from foraging bees and pollen from foraging bees were: 6629, < LOQ (1 µg a.i./kg), < LOD (0.5 µg a.i./kg) and 1.88 µg a.i./kg, respectively. 7-day mean measured residues in leaves and nectar from foraging bees were: 1984 µg a.i./kg and < LOD, respectively. 4-day mean measured residues in pollen from foraging bees were 4.4 µg a.i./kg. Group 2: Peak measured residues in leaves, nectar from foraging bees and pollen from foraging bees were: 4719, < LOD and 72.8 µg a.i./kg, respectively. 7-day mean measured residues in leaves, nectar from foraging bees and pollen were: 2068, 0.63 and 24.8 µg a.i./kg, respectively. Group 3: Peak measured residues in leaves, nectar from foraging bees and pollen from foraging bees were: 25821, 2.04 and 4378 µg a.i./kg, respectively. 7-day mean measured residues in leaves and nectar from foraging bees were: 8260 and 1.19 µg a.i./kg, respectively. 4-day mean measured residues in pollen from foraging bees were 2222.1 µg a.i./kg.	

Study design	Results and overall conclusions	PMRA No.
	Trial 2: Residues were only measured in leaves and nectar from foraging bees during the exposure period of the study. Peak measured residues in leaves and nectar from foraging bees were: 8291 and 1.58 µg a.i./kg, respectively. 6-day mean measured residues in leaves and nectar from foraging bees were: 6672 and 0.86 µg a.i./kg, respectively.	
Test species: Honey bees (*Apis mellifera*) Test Substance: A21708F 100DC Formulated Product (9.25% isocycloseram) Application rate: Group 1: 62.2 g a.i./ha Group 2: 90.7 g a.i./ha Group 3: 124.2 g a.i./ha Reference chemical rate: 300 g fenoxycarb/ha Crop: lacy phacelia (*Phacelia tanacetifolia*) Attractiveness: High Application type and timing: Foliar spray during full flowering applied 4 days after the hives were placed in the tunnels at nightfall after active foraging and bee flight. Exposure and observation length: Colonies were exposed in tunnels for 7 days, with an additional 53 days observation period. Replicates: 4 tunnels per treatment with 1 colony per tunnel. Observed bee/colony health parameters: mortality, foraging activity, behavior	There were no lasting adverse effects for brood termination rate, brood index and brood complex index observed in the bee colonies when isocycloseram was applied at night after active bee foraging and flight at application rates of 62.2 g a.i./ha and 90.7 g a.i./ha. However, a transient statistically significant reduction in brood termination rate, brood index and brood compensation index were observed on 3 DAT (days after treatment) in the 62.2 and 90.7 g a.i./ha treatment groups. No other statistically significant effects on colony strength, food stores, brood termination rates, brood index or brood compensation index were observed on any other days up until study termination (53 DAT) in the 62.2 and 90.7 g a.i./ha treatment groups. No statistically-significant reduction in colony strength was observed in the 62.2 or the 90.7 g a.i./ha treatment groups. There was no statistically significant differences in adult mortality or foraging between the control and the 60 g a.i./ha, 90 g a.i./ha or 124 g	3246153

Study design	Results and overall conclusions	PMRA No.
abnormalities, brood development, and brood termination rate. Residue collection: Yes.	a.i./ha groups during the exposure phase. Residue analysis results: Maximum residues in leaves, pollen from foraging honey bees and nectar from foraging honey bees were: 6.46, 12.2 and 0.069 mg a.i./kg, respectively, for group 1, 10.2, 5.67 and 0.078 mg a.i./kg, respectively, for group 2, and 12.7, 15.2 and 0.072 mg a.i./kg, respectively, for group 3. 7-day mean measured residues in leaves, pollen from foraging honey bees and nectar from foraging honey bees were: 4.4, 3.28 and 0.02 mg a.i./kg, respectively, for group 1, 5.68, 2.41 and 0.04 mg a.i./kg, respectively, for group 2 and 7.73, 4.04 and 0.03 mg a.i./kg, respectively, for group 3.	

Table 19 Toxicity to non-target aquatic species

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
Water flea *(Daphnia magna)*	Isocycloseram Technical (Purity: 96.9%)	48-hour acute (static renewal)	48-h EC_{50}: 460.0 µg a.i./L	Highly toxic	3246160
		21-day chronic (static renewal)	21-d $NOEC_{growth}$: 0.030 µg a.i./L	N/A	3246187
		21-day chronic (static renewal)	21-d NOEC: Not determined (< 0.063 µg a.i./L)	N/A	3246188
	SYN547950 (transformation product of isocycloseram, identified as SYN549107 in fate studies)	48-hour acute (static renewal)	48-h LC_{50}: > 955.0 µg/L	No effects observed at the highest concentration	3246161

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
	SYN549433 (transformation product of isocycloseram)	48-hour acute (static renewal)	48-h LC_{50}: > 80 µg/L	No effects observed at the highest concentration endpoint	3246162
	SYN550455 (transformation product of isocycloseram)	48-hour acute (static renewal)	48-h LC_{50}: > 982 µg/L	No effects observed at the highest concentration endpoint	3246163
	SYN550918 (transformation product of isocycloseram, identified as SYN550738 in fate studies)	48-hour acute (static renewal)	48-h LC_{50}: 166 µg/L	Highly toxic	3246164
	SYN551513 (transformation product of isocycloseram, identified as SYN550603 in fate studies)	48-hour acute (static)	48-h LC_{50}: > 975 µg/L	No effects observed at the highest concentration	3246165
	SYN551754 (transformation product of isocycloseram identified as SYN550602 in fate studies)	48-hour acute (static)	48-h LC_{50}: > 928 µg/L	No effects observed at the highest concentration	3246166
Freshwater midge *(Chironomus riparius)*	Isocycloseram Technical (TGAI Purity: 96.9%)	48-hour acute without sediment (static)	48-h LC_{50}: 0.014 µg a.i./L	Very highly toxic	3246170
		28-day chronic spiked sediment (static)	28-day NOEC: Not determined	N/A	3246192
	SYN547950 (transformation product of isocycloseram, identified as SYN549107 in fate studies)	48-hour acute without sediment (static)	48-h LC_{50}: 51 µg/L	Very highly toxic	3246171

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
	SYN549431 (transformation product of isocycloseram)	48-hour acute without sediment (static)	48-h LC_{50}: 0.29 µg/L	Very highly toxic	3246172
	SYN549433 (transformation product of isocycloseram)	48-hour acute without sediment (static)	48-h LC_{50}: 161 µg/L	Highly toxic	3246173
	SYN549546 (transformation product of isocycloseram)	48-hour acute without sediment (static)	48-h LC_{50}: 829 µg/L	Highly toxic	3246174
	SYN550455 (transformation product of isocycloseram)	48-hour acute without sediment (static)	48-h LC_{50}: 2053 µg/L	Moderately toxic	3246175
	SYN550918 (transformation product of isocycloseram, identified as SYN550738 in fate studies)	48-hour acute without sediment (static)	48-h LC_{50}: 0.81 µg/L	Very highly toxic	3246176
	SYN551113 (transformation product of isocycloseram)	48-hour acute without sediment (static)	48-h LC_{50}: > 977 µg/L	No effects observed at the highest concentration	3246177
	SYN551513 (transformation product of isocycloseram, identified as SYN550603 in fate studies)	48-hour acute without sediment (static)	48-h LC_{50}: 816 µg/L	Highly toxic	3246178
	SYN551753 (transformation product of isocycloseram, identified as SYN550737 in fate studies)	48-hour acute without sediment (static)	48-h LC_{50}: 9.0 µg/L	Very highly toxic	3246179
	SYN551754 (transformation product of isocycloseram)	48-hour acute without sediment (static)	48-h LC_{50}: 644.0 µg/L	Highly toxic	3246180
Freshwater midge *(Chironomus dilutus)*	Isocycloseram Technical (Purity: 96.9%)	60-day chronic	60-d $NOEC_{emergence}$: 0.0013 µg a.i./L	N/A	3246193

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
		spiked sediment (Intermittent-renewal)	(60-d time-weighted measured pore water) 60-d LOEC: 0.0045 µg a.i./L (60-d time-weighted measured pore water) ↓ 39% dry weight ↓ 16% development rate ↓ 21% emergence		
Rotifer *(Brachionus calyciflorus)*	Isocycloseram Technical (Purity: 96.9%)	24-hour acute (static)	24-h LC_{50}: > 785 µg a.i./L	No effects observed at the highest concentration	3246181
Water louse *(Caecidotea communis)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static-renewal)	96-h LC_{50}: 0.145 µg a.i./L	Very highly toxic	3246182
Grass shrimp *(Palaemonetes paludosus)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static-renewal)	96-h LC_{50}: 0.24 µg a.i./L	Very highly toxic	3246183
Beavertail fairy shrimp *(Thamnocephalus platyurus)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static renewal)	96-h LC_{50}: 0.24 µg a.i./L	Very Highly Toxic	3246185
Northern crayfish *(Faxonius virilis)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static-renewal)	96-h LC_{50}: 1.6 µg a.i./L	Very highly toxic	3246184
Caddisfly *(Pycnopsyche gentilis)*	Isocycloseram Technical (Purity: 96.9%)	48-hour acute (static)	48-h LC_{50}: 0.47 µg a.i./L	Very highly toxic	3246168
Mayfly *(Hexagenia limbata)*	Isocycloseram Technical (Purity: 96.9%)	48-hour acute (static)	48-h LC_{50}: 0.32 µg a.i./L	Very highly toxic	3246169
Amphipod *(Hyalella azteca)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static-renewal)	96-h LC_{50}: 0.04 µg a.i./L	Very highly toxic	3246186

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
	Isocycloseram Technical (Purity: 96.9%)	42-day chronic 28-d exposure period, 14-d post exposure observation period Spiked sediment (Intermittent-renewal)	28-d $NOEC_{growth}$: 0.0048 µg a.i./L (28-d mean measured pore water)	N/A	3246195
Freshwater fish					
Rainbow trout *(Oncorhynchus mykiss)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (flow-through)	96-h LC_{50}: 120 µg a.i./L	Highly toxic	3246155
Carp *(Cyprinus carpio)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (flow-through)	96-h LC_{50}: 359 µg a.i./L	Highly toxic	3246156
Fathead minnow *(Pimephales promelas)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (flow-through)	96-h LC_{50}: 320 µg a.i./L	Moderately toxic	3246157
		33-day early life-stage (flow-through)	33-d $NOEC_{growth}$: 107 µg a.i./L	N/A	3246158
Amphibians					
Rainbow trout *(Oncorhynchus mykiss)* Used as surrogate	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (flow-through)	96-h LC_{50}: 120 µg a.i./L	N/A	3246155
Freshwater vascular plants					
Duckweed *(Lemna gibba)*	Isocycloseram Technical (Purity: 96.9%)	7-day (static-renewal)	7-d EC_{50}: > 1100 µg a.i./L A mean reduction of 31% for yield was observed at the highest concentration tested	N/A	3246196
Freshwater algae					
Green algae *(Pseudokirchneriella subcapitata)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static)	96-h EC_{50}: > 1400 µg a.i./L (initial measured) 5% reduction in yield was	N/A	3246189

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
			observed at the highest concentration tested		
Cyanobacteria *(Anabaena flos-aquae)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static)	96-h EC_{50}: > 1400 µg a.i./L (initial measured) No adverse effects were observed up to the highest concentration tested	N/A	3246190
Diatom *(Navicula pelliculosa)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static)	96-h $EC_{50\ Yield}$: 640 µg a.i./L (initial measured)	N/A	3246191
Marine invertebrates					
Mysid shrimp *(Americamysis bahia)*	Isocycloseram Technical (Purity: 96.9%)	96-hour acute (static renewal)	96-h LC_{50}: 0.018 µg a.i./L	Very Highly Toxic	3246137
		28-day chronic (intermittent renewal)	28-d $NOEC_{repro}$: 0.0042 µg a.i./L $LOEC_{repro}$: 0.0071 µg a.i./L ↓ 39% in offspring ↓ 27% in F0 survival ↓ 6.1% in F1 survival	N/A	3246138
Eastern oyster *(Crassostrea virginica)*	Isocycloseram (TGAI Purity: 96.9%)	96-hour acute (flow-through)	96-h EC_{50}: 73 µg a.i./L	Very Highly Toxic	3246139
Estuarine amphipod *(Leptocheirus plumulosus)*	Isocycloseram (TGAI Purity: 96.9%)	28-day intermittent-renewal (spiked sediment)	28-d $NOEC_{weight\ and\ survival}$: 0.0037µg a.i./L (28-d time-weighted mean measured pore water) 28-d $LOEC_{weight\ and\ survival}$:	N/A	3246194

Organism	Test substance	Exposure	Endpoint value	Effects/Degree of toxicity[1]	PMRA No.
			0.0096 µg a.i./L (28-d time-weighted mean measured pore water) based on a 41.4% reduction in survival compared to pooled controls.		
Marine fish					
Sheepshead minnow *(Cyprinodon variegatus)*	Isocycloseram (TGAI Purity: 96.9%)	96-hour acute (flow-through)	96-h LC_{50}: 280 µg a.i./L	Highly toxic	3246140
		34 day early life-stage (flow-through)	34-d $NOEC_{weight}$: 7.8 µg a.i./L	N/A	3246142
Marine algae					
Saltwater diatom *(Skeletonema costatum)*	Isocycloseram (TGAI Purity: 96.9%)	96-hour acute (static)	96-h EC_{50}: 395 µg a.i./L	N/A	3246141

[1] USEPA classification, where applicable

N/A = not available

Table 20 Screening level risk assessment for non-target terrestrial organisms (excluding birds and small wild mammals) from foliar spray

Organism	Test substance	Exposure type	EEC	Endpoint value	UF	Effects metric	RQ	LOC	LOC of 0.4, 1 or 2 exceeded?
Invertebrates									
Soil dwelling organisms									
Earthworm (*Eisenia fetida*)	Isocyclosera m (Purity 96.9%)	14-d acute	0.02 mg a.i./kg soil dw	> 969 mg a.i./kg soil dw	2	> 484	0.00004	1	No
		56-d chronic	0.02 mg a.i./kg soil dw	10 mg a.i./kg soil dw	1	10	0.002	1	No
Collembolan (*Folsomia candida*)	Isocyclosera m (Purity 98.4%)	28-day $EC_{50reproduction}$	0.02 mg a.i./kg soil dw	0.217 mg a.i./kg soil dw	1	0.217	0.1	1	No
		28-day $NOEC_{reproduction}$	0.02 mg a.i./kg soil dw	0.095 mg a.i./kg soil dw	1	0.095	0.2	1	No
Predatory Mite (*Hypoaspis aculeifer*)	Isocyclosera m Technical Purity: 98.4% w/w	14-day artificial soil LC_{50}	0.02 mg a.i./kg soil dw	0.821 mg a.i./kg soil dw	1	0.821	0.02	1	No
		14-day artificial soil $EC_{50\ reproduction}$	0.02 mg a.i./kg soil dw	0.343 mg a.i./kg soil dw	1	0.343	0.06	1	No
		14-day artificial soil $NOEC_{reproduction}$	0.02 mg a.i./kg soil dw	0.171 mg a.i./kg soil dw	1	0.171	0.1	1	No
	SYN547950 (transformatio n product of	14-day artificial soil LC_{50}	0.016 mg a.i./kg soil dw	25 mg/kg dw soil dw	1	25	0.001	1	No

Organism	Test substance	Exposure type	EEC	Endpoint value	UF	Effects metric	RQ	LOC	LOC of 0.4, 1 or 2 exceeded?
	isocycloseram)	14-day artificial soil $EC_{50\ reproduction}$	0.016 mg a.i./kg soil dw	20.8 mg/kg soil dw	1	20.8	0.001	1	No
		14-day artificial soil $NOEC_{reproduction}$	0.016 mg a.i./kg soil dw	5.8 mg/kg soil dw	1	5.8	0.003	1	No
	SYN549433 (transformation product of isocycloseram)	14-day artificial soil LC_{50}	0.02 mg a.i./kg soil dw	> 61.2 mg/kg soil dw	1	61.2	< 0.003	1	No
		14-day artificial soil $EC_{50\ reproduction}$	0.02 mg a.i./kg soil dw	> 61.2 mg/kg soil dw	1	61.2	< 0.003	1	No
		14-day artificial soil $NOEC_{reproduction}$	0.02 mg a.i./kg soil dw	34.0 mg/kg soil dw	1	34.0	0.0006	1	No
	SYN550918 (transformation product of isocycloseram)	14-day artificial soil LC_{50}	0.016 mg a.i./kg soil dw	> 61.2 mg/kg soil dw	1	61.2	< 0.003	1	No
		14-day artificial soil $EC_{50\ reproduction}$	0.016 mg a.i./kg soil dw	> 61.2 mg/kg soil dw	1	61.2	< 0.003	1	No
		14-day artificial soil $NOEC_{reproduction}$	0.016 mg a.i./kg soil dw	> 61.2 mg/kg soil dw	1	10.5	0.0015	1	No
Foliar dwelling organisms									
Bee	Isocycloseram (Purity 96.9%)	72-h adult acute oral	1.431 µg a.i./bee/day	0.29 µg a.i./bee/day	1	0.28	5.1	0.4	Yes
		96-h adult acute contact	0.12 µg a.i./bee/day	0.26 µg a.i./bee/day	1	0.26	0.5	0.4	Yes
		72-h larval single exposure	4.9 mg a.i./kg diet	3.88 mg a.i./kg diet	1	0.1	1.3	0.4	Yes

Organism	Test substance	Exposure type		EEC	Endpoint value	UF	Effects metric	RQ	LOC	LOC of 0.4, 1 or 2 exceeded?
		22-d larval repeated exposure		4.9 mg a.i./kg diet	0.10 mg a.i./kg diet	1	0.1	49	1	Yes
		10-d adult chronic		4.9 mg a.i./kg diet	0.11 mg a.i./kg diet	1	0.11	45	1	Yes
	SYN549106 (transformation product of Isocyclosera m)	96-h adult acute oral		1.13 µg a.i./bee	0.18 µg a.i./bee	1	0.18	6.3	0.4	Yes
		96-h adult acute contact		0.095 µg a.i./bee	0.072 µg a.i./bee	1	0.072	1.3	0.4	Yes
Predatory arthropod *(Typhlodromus pyri)*	SYN547407 DC 100 formulated product (100 g a.i./L Isocyclosera m)	7-d LR_{50} Contact (glass plate)	On-field Turf	50 g a.i./ha	0.0059 g a.i./ha	1	0.0059	8475	2	Yes
			On-field Orchard and other crops	32.3 g a.i./ha	0.0059 g a.i./ha	1	0.0059	5474	2	Yes
			Off-field Turf	3.0 g a.i./ha	0.0059 g a.i./ha	1	0.0059	508	2	Yes
			Off-field Orchard	23.9 g a.i./ha	0.0059 g a.i./ha	1	0.0059	4051	2	Yes
Parasitoid wasp (*Aphidius rhopalosiphi*)	SYN547407 DC 100 (Formulated product) Purity: 9.29% w/w	48-h LR_{50} Contact (glass plate)	On-field Turf	50 g a.i./ha	0.42 g a.i./ha	1	0.42	119	2	Yes
			On-field Orchard and other crops	32.3 g a.i./ha	0.42 g a.i./ha	1	0.42	77	2	Yes
			Off-field Turf	3.0 g a.i./ha	0.42 g a.i./ha	1	0.42	7	2	Yes
			Off-field Orchard	23.9 g a.i./ha	0.42 g a.i./ha	1	0.42	57	2	Yes
Vascular plants										
		Single application		50 g a.i./ha	818 g a.i./ha	1	818	0.1	1	No

Organism	Test substance	Exposure type	EEC	Endpoint value	UF	Effects metric	RQ	LOC	LOC of 0.4, 1 or 2 exceeded?
Vascular plants	Isocycloseram SC formulated product (200 g/L isocycloseram)	ER_{25} Seedling emergence							
		Single application ER_{25} Vegetative vigour	50 g a.i./ha		1		0.1		No

Table 21 Refined risk assessment for non-target terrestrial organisms (excluding birds, small wild mammals and bees) from foliar spray

Organism	Test substance	Exposure type		EEC (g a.i./ha)	Effects metric	UF	RQ	LOC	LOC of 1 exceeded ?
Turf									
Predatory arthropod *(Typhlodromus pyri)*	SYN547407 DC 100 formulated product (100 g a.i./L Isocycloseram)	7-d LR_{50} Contact (Dried residues on foliage)	On-field (40% foliar deposition)	20	0.0072 g a.i./ha	1	2778	1	Yes
			Off-field (with 6% drift and 10% vegetation distribution)	0.30	0.0072 g a.i./ha	1	42	1	Yes
		14-d reproduction ER_{50} Contact (Dried residues on foliage)	On-field (40% foliar deposition)	20	0.006 g a.i./ha	1	3333	1	Yes
			Off-field (with 6% drift and 10% vegetation distribution)	0.30	0.006 g a.i./ha	1	50	1	Yes
			On-field	20	2.46 g a.i./ha	1	8	1	Yes

Organism	Test substance	Exposure type		EEC (g a.i./ha)	Effects metric	UF	RQ	LOC	LOC of 1 exceeded ?
Parasitoid wasp (*Aphidius rhopalosiphi*)	SYN547407 DC 100 formulated product (100 g a.i./L Isocyclosera m)	48-h LR_{50} Contact (Dried residues on foliage) (13 day study)	(40% foliar deposition)						
			Off-field (with 6% drift and 10% vegetation distribution)	0.30	2.46 g a.i./ha	1	0.1	1	No
		13-d reproductio n ER_{50}: > 2.44 A 13-day ER_{50} reproductio n could not be determined due to high adult mortality in the test vessels above 2.44 g a.i./ha.	On-field (40% foliar deposition)	20	> 2.44 g a..i./ha	1	< 8	1	Yes
			Off-field (with 6% drift and 10% vegetation distribution)	0.30	> 2.44 g a..i./ha	1	< 0.1	1	No
Risk to foliar dwelling benefical arthropods from use on pome fruit (orchard crops) (20 g a.i./ha × 2 with 7-d intervals)									
Predatory arthropod *(Typhlodro mus pyri)*	SYN547407 DC 100 formulated product	7-d LR_{50} Contact (Dried residues on foliage)	On-field (80% foliar deposition)	21.7	0.0072 g a.i./ha	1	3014	1	Yes
			Off-field	2.0	0.0072 g a.i./ha	1	278	1	Yes

Organism	Test substance	Exposure type		EEC (g a.i./ha)	Effects metric	UF	RQ	LOC	LOC of 1 exceeded ?
	(100 g a.i./L Isocyclosera m)		(with 74% drift and 10% vegetation distribution)						
		14-d Reproductio n ER_{50} Contact (Dried residues on foliage)	On-field (80% foliar deposition)	21.7	0.006 g a.i./ha	1	3617	1	Yes
			Off-field (with 74% drift and 10% vegetation distribution)	2.0	0.006 g a.i./ha	1	333	1	Yes
Parasitoid wasp (*Aphidius rhopalosiph i*)	SYN547407 DC 100 formulated product (100 g a.i./L Isocyclosera m)	48-h LR_{50} Contact (Dried residues on foliage) (13 day study)	On-field (80% foliar deposition)	21.7	2.46 g a.i./ha	1	9	1	Yes
			Off-field (with 74% drift and 10% vegetation distribution)	2.0	2.46 g a.i./ha	1	0.8	1	No
		13-d Reproductio n ER_{50}: > 2.44 A 13-day ER_{50} reproduction could not be determined due to high adult mortality in the test	On-field (80% foliar deposition)	21.7	> 2.44 g a..i./ha	1	< 9	1	Yes
			Off-field (with 74% drift and 10% vegetation distribution)	2.0	> 2.44 g a..i./ha	1	< 0.9	1	No

Organism	Test substance	Exposure type		EEC (g a.i./ha)	Effects metric	UF	RQ	LOC	LOC of 1 exceeded ?
		vessels above 2.44 g a.i./ha.							
Risk to foliar dwelling benefical arthropods from other field crops (20 g a.i./ha × 2 with 7-day intervals)									
Predatory arthropod *(Typhlodromus pyri)*	SYN547407 DC 100 formulated product (100 g a.i./L Isocyclosera m)	7-d LR_{50} Contact (Dried residues on foliage)	On-field (80% foliar deposition)	21.7	0.0072 g a.i./ha	1	3014	1	Yes
			Off-field (with 6% drift and 10% vegetation distribution)	0.16	0.0072 g a.i./ha	1	22	1	Yes
		14-d reproductio n ER_{50} Contact (Dried residues on foliage)	On-field (80% foliar deposition)	21.7	0.006 g a.i./ha	1	3617	1	Yes
			Off-field (with 6% drift and 10% vegetation distribution)	0.16	0.006 g a.i./ha	1	27	1	Yes
Parasitoid wasp (*Aphidius rhopalosiphi*)		48-h LR_{50} Contact (Dried residues on foliage)(13-day study)	On-field (with 80% deposition)	21.7	2.46 g a.i./ha	1	9	1	Yes
			Off-field (with 6% drift and 10% vegetation distribution)	0.16	2.46 g a.i./ha	1	0.07	1	No
		13-d reproductio n ER_{50}: > 2.44	On-field (with 80% deposition)	21.7	> 2.44 g a..i./ha	1	< 9	1	Yes
			Off-field	0.16	> 2.44 g a..i./ha	1	< 0.07	1	No

Organism	Test substance	Exposure type		EEC (g a.i./ha)	Effects metric	UF	RQ	LOC	LOC of 1 exceeded ?
		A 13-day ER_{50} reproduction could not be determined due to high adult mortality in the test vessels above 2.44 g a.i./ha.	(with 6% drift and 10% vegetation distribution)						

Table 22 Number of days required for the EEC to drop below the effects metrics for predatory mites and parasitic wasps in refined assessment

Use pattern	Number of applications[1]	Initial day 0 EEC[2]	Number of days for EEC to drop below effect metric for predatory mite (0.006 g a.i./ha)[3]	Number of days for EEC to drop below effect metric for parasitic wasp (2.46 g a.i./ha)[3]
Turf on-field	1	20 g a.i./ha	55	14
Turf off-field	1	0.3 g a.i./ha	27	0
Orchard and other field crops on-field	1	16 g a.i./ha	56	16
Orchard and other field crops on-field	2	16 g a.i./ha	108	26
Orchard off-field	1	1.5 g a.i./ha	40	0
Orchard off-field	2	1.5 g a.i./ha	76	0
Other field crops off-field	1	0.12 g a.i./ha	23	0
Other field crops off-field	2	0.12 g a.i./ha	40	0

[1] For multiple applications, there is no specified maximum time between applications, the second application is made based on the residual time to reach the effects metric for both mites and wasps. As such, they are different depending on effects metrics. For orchard and field crops, EECs are based on the single highest rate is 20 g a.i./ha for one application scenario.

[2] Initial day 0 EECs are calculated based on the rate of application with incorporation of on-field foliar deposition fractions and off-field spray drift deposition plus vegetation distribution factors. For multiple applications, the half-life between applications is 4.7 days and the re-application occurs any time during the season.

[3] The number of days required for the EEC to drop below the effect metric can be calculated based on a DT_{50} of 4.7 days and using the following equation:
$EEC_x = EEC_i \cdot e^{-0.147x}$
Where, $x = \frac{\ln(EEC_i/EEC_x)}{0.147}$
EEC_x represents the effect metric after X number of days
EEC_i represents the initial EEC
k=ln(2)DT_{50}=0.6934.7≈0.147k = \frac{\ln(2)}{\{DT_{50}} = \frac{0.693}{4.7}\approximately 0.147k=DT_{50}ln(2)=4.70.693≈0.147
0.147 is the rate constant for DT_{50} = 4.7 days.

Table 23 Refined risk assessment for pollinators

Test substance	Exposure type	Expected exposure/EDD/EDE	Effect metric	RQ	LOC	LOC of 0.4 or 1 exceeded?
Orchard and field crop rates (Single highest rate of 30 g a.i./ha)						
Isocycloseram (Purity 96.9%)	72-h adult acute oral	0.858 µg a.i./bee	0.29 µg a.i./bee	3	0.4	Yes
	96-h adult acute contact	0.072 µg a.i./bee	0.26 µg a.i./bee	0.3	0.4	No
	72-h larval single exposure	2.9 mg a.i./kg diet	3.88 mg a.i./kg diet	0.8	0.4	Yes
	22-d larval repeated exposure	2.9 mg a.i./kg diet	0.10 mg a.i./kg diet	29	1	Yes
	10-d adult chronic	2.9 mg a.i./kg diet	0.11 mg a.i./kg diet	27	1	Yes
SYN549106 (metabolite of isocycloseram)	96-h adult acute oral	0.678 µg a.i./bee	0.18 µg a.i./bee	3.8	0.4	Yes
	96-h adult acute contact	0.057 µg a.i./bee	0.072 µg a.i./bee	0.079	0.4	Yes

Table 24 Further characterization of risks using maximum measured concentrations of isocycloseram in pollen and nectar, compared with Tier I laboratory effects metrics

Crop	Number of applications and application rates and timing	Concentration in pollen (mg a.i./kg)	Concentration in nectar (mg a.i./kg)	Acute oral adult (0.29 µg/bee) RQ	Chronic oral adult (0.11 mg a.i./kg diet) RQ	Acute oral larva (3.88 mg a.i./kg diet) RQ	Chronic oral larva (0.1 mg a.i./kg diet) RQ	PMRA No.
Residues collected from plants								
Cotton	3 × 40 g a.i./ha (during bloom during bee flight)	Max: 0.414 Mean: 0.038	Max: 0.833 Mean: 0.1085	0.83	0.98	0.21	1.1	3246147
Cotton	1 × 82 g a.i./ha (during bloom during bee flight)	Max: 0.103 Mean: 0.037	Max: 0.237 Mean: 0.1377	0.24	1.3	0.06	1.4	3246148
Residues collected from bees and plants								
Soybean *	3 apps (40, 40, 69.9 g a.i./ha) during bloom during bee flight	Max (anther): 1.78 Mean (anther): 0.574	Max: 0.0255 Mean: 0.0117 (forager bees)	0.026	0.11	0.02	0.28	3246154
Residues collected from bees								
Niger	Group 1: One application of 41.6 g a.i./ha applied 1 day prior to bee colonies being placed in the exposure tunnels followed by two consecutive applications of 89.5 g a.i./ha each applied in the evening after active bee foraging and flight.	Max: 5.2 (forager bees) Max: 2.48 (pollen traps) Mean: 2.4 (forager bees) Mean: 0.767 (pollen traps)	Max: 0.044 Mean: 0.013	0.045	0.12	0.05	0.85	3246149
	Group 2: One application of 39.9 g a.i./ha applied 1 day prior to bee colonies being placed in the exposure tunnels followed by one application of 90.6 g	Max: 3.2 (forager bees) Max: 1.06 (pollen traps) Mean: 1.5 (forager bees)	Max: 0.041 Mean: 0.012	0.04	0.11	0.034	0.53	

Crop	Number of applications and application rates and timing	Concentration in pollen (mg a.i./kg)	Concentration in nectar (mg a.i./kg)	Acute oral adult (0.29 µg/bee) RQ	Chronic oral adult (0.11 mg a.i./kg diet) RQ	Acute oral larva (3.88 mg a.i./kg diet) RQ	Chronic oral larva (0.1 mg a.i./kg diet) RQ	PMRA No.
	a.i./ha in the evening after active bee foraging and flight followed by the third and final application of 88.1 g a.i./ha applied in the morning before active bee foraging and flight.	Mean: 0.45 (pollen traps)						
Phacelia	Group 1: 60 g a.i./ha applied during bloom 3 days after hives were placed in tunnels at nightfall	Max: 12 (forager bees) Mean: 3.3 (forager bees)	Max: 0.069 Mean: 0.02	0.07	0.19	0.11	1.2	3246153
	Group 2: 90 g a.i./ha applied during bloom 3 days after hives were placed in tunnels at nightfall	Max: 5.67 (forager bees) Mean: 2.41 (forager bees)	Max: 0.078 Mean: 0.04	0.08	0.37	0.06	1.1	
	Group 3: 120 g a.i./ha applied during bloom 3 days after hives were placed in tunnels at nightfall	Max: 15.2 (forager bees) Mean: 4.04 (forager bees)	Max: 0.072 Mean: 0.03	0.07	0.28	0.13	1.5	

*There was heavy rain in this study and no effects in the dimethoate group, suggesting low exposure from residues in the study. However, residues were detected and included here for consideration.
Note: pollen and nectar collected from plants unless otherwise stated.

Table 25 Further risk characterization to bees using mean measured concentrations of isocycloseram in pollen and nectar, and a comparison with sucrose dosed colony feeding study NOEC (0.28 mg a.i./kg)

Crop	Number of applications and application rates and timing	Mean concentration in pollen (mg a.i./kg)	Mean concentration in nectar (mg a.i./kg)	Are pollen residues > CFS NOEC	Are nectar residues > CFS NOEC	PMRA No.
Residues collected from plants						
Cotton	3 × 40 g a.i./ha (during bloom during bee flight)	0.038	0.1085	No	No	3246147
Cotton	1 × 82 g a.i./ha (during bloom during bee flight)	0.037	0.1377	No	No	3246148
Residues collected from bees and plants						
Soybean*	3 apps (40, 40, 69.9 g a.i./ha) during bloom during bee flight	0.574 (anther)	0.0117 (forager bees)	Yes	No	3246154
Residues collected from bees						
Niger	Group 1: One application of 41.6 g a.i./ha applied 1 day prior to bee colonies being placed in the exposure tunnels followed by two consecutive applications of 89.5 g a.i./ha each applied in the evening after active bee foraging and flight.	2.4 (forager bees) 0.767 (pollen traps)	0.013	Yes	No	3246149
	Group 2: One application of 39.9 g a.i./ha applied 1 day prior to bee colonies being placed in the exposure tunnels followed by one application of 90.6 g a.i./ha in the evening after active bee foraging and flight followed by the third and final application of 88.1 g a.i./ha applied in the morning before active bee foraging and flight.	1.5 (forager bees) 0.45 (pollen traps)	0.012	Yes	No	
Phacelia	Group 1: 60 g a.i./ha applied during bloom 3 days after hives were placed in tunnels at nightfall	3.28 (forager bees)	0.02	Yes	No	3246153

Crop	Number of applications and application rates and timing	Mean concentration in pollen (mg a.i./kg)	Mean concentration in nectar (mg a.i./kg)	Are pollen residues > CFS NOEC	Are nectar residues > CFS NOEC	PMRA No.
	Group 2: 90 g a.i./ha applied during bloom 3 days after hives were placed in tunnels at nightfall	2.41 (forager bees)	0.04	Yes	No	
	Group 3: 120 g a.i./ha applied during bloom 3 days after hives were placed in tunnels at nightfall	4.04 (forager bees)	0.03	Yes	No	

* There was heavy rain in this study and no effects in the dimethoate group, suggesting low exposure from residues in the study. However, residues were detected and included here for consideration.

Note: pollen and nectar collected from plants unless otherwise stated.

Table 26 Crop-specific pollinator mitigation requirements for foliar applications

Crop	Pollinator exposure (crop-based)	Application rate (pollinator protection level)[1]	Mitigation required on label
Outdoor uses			
Potato	Low	50 g a.i./ha (moderate)	**Moderately restrictive pollinator protection level:** Avoid application during bloom. If applications must be made during blooming period, restrict applications to the evening.
Tuberous and Corm Vegetables (Crop Subgroup 1C)	Negligible (harvested before bloom)		
Leafy Vegetables (Group 4-13) Except head lettuce	Negligible (harvested before bloom)		
Brassica Leafy Greens (Group 4-13B)	Negligible (harvested before bloom)		
Brassica Head and Stem Vegetables (Group 5-13)	Negligible (harvested before bloom)		
Fruiting Vegetables (Group 8-09)	Moderate		
Cucurbit Vegetables (Group 9)	High		

Crop	Pollinator exposure (crop-based)	Application rate (pollinator protection level)[1]	Mitigation required on label
Pome Fruits (Group 11-09)	High		
Stone Fruits (Group 12-09)	High		
Tree Nuts	Negligible to high - varies by tree type (for example, **High:** almond, chestnut, chinquapin, Japanese horse-chestnut; **Low/Moderate:** beechnut, black walnut, bur oak, butternut, English walnut, hazelnut, heartnut, yellowhorn, hickory nut; **Negligible:** gingko, pecan, pine nut, monkey puzzle nut.)		
Soybeans	Low to moderate		
Peanuts	Low		
Corn	Moderate		
Turf (sod and lawns) [turfgrass sites such as sod farms, golf courses, parks and recreational areas, athletic fields, home and residential lawns, industrial and commercial lawns, airports and cemeteries]	Sod and golf courses: Negligible (managed for weeds) Lawns: High if containing flowering weeds such as clover, dandelions, etc.	50 g a.i./ha (moderate)	**Moderately restrictive pollinator protection level:** Avoid application when bees are foraging in the treatment area in ground cover containing blooming weeds. If applications must be made in areas that contain blooming plants or weeds, restrict applications to the evening.
Greenhouse uses			
Ornamentals (Greenhouse, could be moved outside)	High	150 g a.i./ha (high)	**Most restrictive pollinator protection level**: Avoid application when bees are in the treatment area. Additionally, greenhouse

Crop	Pollinator exposure (crop-based)	Application rate (pollinator protection level)[1]	Mitigation required on label
			plants sprayed during bloom should not be moved outdoors while the sprayed blooms remain on the plant.

[1] The application rate influenced the risk characterization and the required level of pollinator protection: 50 g a.i./ha - moderately restrictive pollinator protection; 150 g a.i./ha: most restrictive pollinator protection.

Table 27 Screening level risk assessment for birds and small wild mammals from foliar spray on turf at 50 g a.i./ha

Organism	Effects metric[1] (mg a.i./kg bw/d)	Feeding guild (food item)	EDE[2] (mg a.i./kg bw)	RQ	LOC	LOC of 1 exceeded?
Small-sized bird (0.02 kg)						
Acute dietary	46.60	Insectivore	4.1	0.1	1	No
Reproduction	14.60	Insectivore	4.1	0.3	1	No
Medium-sized bird (0.1 kg)						
Acute dietary	46.60	Insectivore	3.2	0.1	1	No
Reproduction	14.60	Insectivore	3.2	0.2	1	No
Large-sized bird (1 kg)						
Acute oral	46.60	Herbivore (short grass)	2.1	0.04	1	No
Reproduction	14.60	Herbivore (short grass)	2.1	0.1	1	No
Small-sized small wild mammal (0.015 kg)						
Acute oral	500.00	Insectivore	2.3	0.005	1	No
Reproduction	3.50	Insectivore	2.3	0.7	1	No
Medium-sized small wild mammal (0.035 kg)						
Acute oral	500.00	Herbivore (short grass)	4.5	0.01	1	No
Reproduction	3.50	Herbivore (short grass)	4.5	1.3	1	Yes
Large-sized small wild mammal (1 kg)						
Acute oral	500.00	Herbivore (short grass)	2.4	0.005	1	No
Reproduction	3.50	Herbivore (short grass)	2.4	0.7	1	No

[1] Uncertainty factors of 10 and 1 were applied to the acute oral (or acute dietary) and reproduction endpoints, respectively.

[2] EDE = Estimated dietary exposure. EDEs were calculated using the following formula: (FIR/body weight) × 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 (body weight in g)$^{0.850}$.
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648 (body weight in g)$^{0.651}$.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235 (body weight in g)$^{0.822}$.
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. The EECs for birds and mammals were calculated based on a single application of 50 g a.i./ha.

Table 28 Further characterization of risk to small wild mammals

Exposure type	Effects metric (mg a.i./kg bw/d)	Feeding guild	Maximum nomogram residues		Mean nomogram residues		LOC	LOC of 1 exceeded? [2]
			EDE[1] (mg a.i./kg bw)	RQ	EDE[1] (mg a.i./kg bw)	RQ		
Medium-sized mammal (0.035 kg)								
On-field								
Reproduction	3.5	Insectivore	2.1	0.6	1.4	0.4	1	No
		Granivore	0.3	0.09	0.2	0.04	1	No
		Frugivore	0.6	0.2	0.3	0.09	1	No
		Herbivore (short grass)	4.5	1.3	1.6	0.5	1	No
		Herbivore (long grass)	2.8	0.8	0.9	0.3	1	No
		Herbivore (forage crops)	4.2	1.2	1.4	0.4	1	No
Off-field (early airblast)								
Reproduction	3.5	Insectivore	1.5	0.4	1.0	0.3	1	No
		Granivore	0.2	0.07	0.1	0.03	1	No
		Frugivore	0.5	0.1	0.2	0.06	1	No
		Herbivore (short grass)	3.4	1.0	1.2	0.3	1	No
		Herbivore (long grass)	2.1	0.6	0.7	0.2	1	No
		Herbivore (forage crops)	3.1	0.9	1.0	0.3	1	No

[1] On-field EDEs were calculated based on the application rate of 50 g a.i./ha. A minimum re-application interval and dissipation between applications was not considered as the use pattern is based on a single application. Off-field EDEs were calculated based on the application rate of 40 g a.i./ha, a 7-day minimum application interval, a default foliar half-life of 10 days and early airblast application method (74% spray drift).

[2] When considering mean nomogram residues.

Table 29 Screening level risk assessment for aquatic organisms from isocycloseram used as a foliar spray (on turf at a rate of 50 g a.i./ha)

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Invertebrates								
Water flea (*Daphnia magna*)	48-h Acute	SYN547950 (transformation product of isocycloseram, identified as SYN549107 in fate studies)	4.97	≥955	2	477.5	0.01	No
	48-h Acute	SYN549433 (transformation product of isocycloseram)	6.28	≥80	2	40	0.2	No
	48-h Acute	SYN550455 (transformation product of isocycloseram)	6.33	≥982	2	491	0.01	No
	48-h Acute	SYN550918 (transformation product of isocycloseram, identified as SYN550738 in fate studies)	5.13	166	2	83	0.1	No
	48-h Acute	SYN551513 (transformation product of isocycloseram, identified as SYN550603 in fate studies)	3.33	≥975	2	487.5	0.01	No

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
	48-h Acute	SYN551754 (transformation product of isocycloseram)	6.31	≥928	2	464	0.01	No
Freshwater midge (*Chironomus riparius*)	48-h Acute	Isocycloseram (TGAI Purity: 96.9%)	6.25	0.014	2	0.007	893	Yes
	48-h Acute	SYN547950 (transformation product of isocycloseram, identified as SYN549107 in fate studies)	4.97	51	2	25.5	0.2	No
	48-h Acute	SYN549431 (transformation product of isocycloseram)	4.96	0.29	2	0.145	34	Yes
	48-h Acute	SYN549433 (transformation product of isocycloseram)	6.28	161	2	80.5	0.1	No
	48-h Acute	SYN549546 (transformation product of isocycloseram)	3.0	829	2	414.5	0.01	No
	48-h Acute	SYN550455 (transformation product of isocycloseram)	6.33	2053	2	1026.5	0.01	No
	48-h Acute	SYN550918 (transformation product of isocycloseram, identified as SYN550738 in fate studies)	5.13	0.81	2	0.405	12.7	Yes
	48-h Acute	SYN551113 (transformation product of isocycloseram)	5.0	≥977	2	488.5	0.01	No

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
	48-h Acute	SYN551513 (transformation product of isocycloseram, identified as SYN550603 in fate studies)	3.33	816	2	408	0.01	No
	48-h Acute	SYN551753 (transformation product of isocycloseram, identified as SYN550737 in fate studies)	6.27	9	2	4.5	1.4	Yes
	48-h Acute	SYN551754 (transformation product of isocycloseram)	6.31	644	2	322	0.02	No
Freshwater midge (*Chironomus dilutes*)	60-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	6.25	0.0013	1	0.0013	4808	Yes
Fish								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	6.25	120	10	12	0.5	No
Fathead minnow (*Pimephales promelas*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	6.25	320	10	32	0.2	No
	33-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	6.25	107	1	10.7	0.1	No
Vascular plants and algae								
Alga (*Navicula pelliculosa*)	96-d Acute	Isocycloseram (TGAI Purity: 96.9%)	6.25	640	2	320	0.02	No

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Vascular plant Duckweed (*Lemna gibba*)	7-d Dissolved	Isocycloseram (TGAI Purity: 96.9%)	6.25	> 1100	2	> 550	< 0.01	No
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	33.3	120	10	12	2.8	Yes
Marine species								
Invertebrates								
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	6.25	0.018	2	0.009	694	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	6.25	0.0042	1	0.0042	1488	Yes
Estuarine amphipod *(Leptocheirus plumulosus)*	21-d Chronic (Spiked sediment)	Isocycloseram Technical (Purity: 96.9%)	6.25	0.0037	1	0.0037	1689	Yes
Fish								
Fish Sheepshead minnow (*Cyprinodon variegatus*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	6.25	280	10	28	0.2	No
	34-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	6.25	7.8	1	7.8	0.8	No
Algae								
Alga *(Skeletonema costatum*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	6.25	395	2	198	0.03	No

Table 30 Refined level risk assessment for aquatic organisms from runoff of isocycloseram used as a foliar spray on turf

Organism	Exposure	Test substance	EEC (µg a.i./L)[1]	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.063	0.04	2	0.02	3.2	Yes
Freshwater midge (*Chironomus riparius*)	48-h Acute (no sediment)	Isocycloseram (TGAI Purity: 96.9%)	0.099	0.014	2	0.007	14	Yes
Freshwater midge (*Chironomus dilutes*)	60-d Chronic spiked sediment	Isocycloseram (TGAI Purity: 96.9%)	0.014	0.0013 (pore water) (NOEC)	1	0.0013	11	Yes
				0.0045[2] (pore water) (LOEC)	1	0.0045	3.1	Yes
			0.005 (pore water)	0.0013 (pore water) (NOEC)	1	0.0013	3.8	Yes
				0.0045[2] (pore water) (LOEC)	1	0.0045	1.1	Yes
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.081	120	10	12	0.007	No
Marine species								
Estuarine amphipod	21-d Chronic		0.005	0.0037 (NOEC)	1	0.0037	1.4	Yes

Organism	Exposure	Test substance	EEC (µg a.i./L)[1]	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
(Leptocheirus plumulosus)	Spiked sediment	Isocycloseram Technical (Purity: 96.9%)	(pore water)	0.0096[3] (LOEC)	1	0.0096	0.5	No
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.063	0.018	2	0.009	7	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	0.027	0.0042 (NOEC)	1	0.0042	6.4	Yes
				0.0071[4] (LOEC)	1	0.0071	3.8	Yes

1 Overlying water unless stated otherwise.
2 LOEC based on 39% reduction in dry weight, 16% redcution in development rate and 21% reduction in emergence.
3 LOEC based 41.4% reduction in surival.
4 LOEC based on 39% reduction in offspring, reduction of 27% in F*0* survival and a reduction of 6.1% in F*1* survival.

Table 31 Refined level risk assessment for aquatic organisms from spray drift 1 m downwind of isocycloseram used as a foliar spray on turf

Organism	Exposure	Test substance	EEC[1] (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.375	0.04	2	0.02	19	Yes
Freshwater midge (*Chironomus riparius*)	48-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.375	0.014	2	0.007	54	Yes
Freshwater midge	60-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	0.375	0.0013 (pore water) (NOEC)	1	0.0013	288	Yes

Organism	Exposure	Test substance	EEC[1] (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
(*Chironomus dilutes*)				0.0045[2] (pore water) (LOEC)	1	0.0045	83	Yes
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	2.0	120	10	12	0.2	No
Marine species								
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.375	0.018	2	0.009	42	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	0.375	0.0042 (NOEC)	1	0.0042	89	Yes
				0.0071[4] (LOEC)	1	0.0071	53	Yes

1 Overlying water unless stated otherwise.
2 LOEC based on 39% reduction in dry weight, 16% redcution in development rate and 21% reduction in emergence.
3 LOEC based 41.4% reduction in survival.
4 LOEC based on 39% reduction in offspring, reduction of 27% in F0 survival and a reduction of 6.1% in F1 survival.

Table 32 Refined level risk assessment for aquatic organisms from runoff of isocycloseram used as a foliar spray on orchard crops

Organism	Exposure (applied in water unless otherwise stated)	Test substance	EEC (µg a.i./L in overlying water unless stated otherwise)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.066	0.04	2	0.02	3.3	Yes
Freshwater midge (*Chironomus riparius*)	48-h Acute (no sediment)	Isocycloseram (TGAI Purity: 96.9%)	0.106	0.014	2	0.007	15	Yes
Freshwater midge (*Chironomus dilutes*)	60-d Chronic Spiked sediment	Isocycloseram (TGAI Purity: 96.9%)	0.012	0.0013 (pore water) (NOEC)	1	0.0013	9.2	Yes
				0.0045[1] (pore water) (LOEC)	1	0.0045	2.7	Yes
			0.004 (pore water)	0.0013 (pore water) (NOEC)	1	0.0013	3.1	Yes
				0.0045[1] (pore water) (LOEC)	1	0.0045	0.9	No
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.069	120	10	12	0.006	No

Organism	Exposure (applied in water unless otherwise stated)	Test substance	EEC (µg a.i./L in overlying water unless stated otherwise)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Marine species								
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.066	0.018	2	0.009	7.3	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	0.023	0.0042 (NOEC)	1	0.0042	5.5	Yes
				0.0071[2] (LOEC)	1	0.0071	3.2	Yes
Estuarine amphipod *(Leptocheirus plumulosus)*	21-d Chronic Spiked sediment	Isocycloseram Technical (Purity: 96.9%)	0.004 (pore water)	0.0037 (NOEC)	1	0.0037	1.1	Yes
				0.0096[3] (LOEC)	1	0.0096	0.4	No

[1] LOEC based on 39% reduction in dry weight, 16% redcution in development rate and 21% reduction in emergence; based on highest test concentration.
[2] LOEC based on 39% reduction in offspring, reduction of 27% in F0 survival and a reduction of 6.1% in F1 survival, based on highest test concentration.
[3] LOEC is set at the highest concentration without significant mortality (which affected ability to assess sublethal effects). Survival LOEC was 0.0096 µg a.i./L based on 41% surival.

Table 33 Refined level risk assessment for aquatic organisms from spray drift 1 m downwind of isocycloseram used as a foliar spray on orchard crops

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	3.66	0.04	2	0.02	183	Yes

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater midge (*Chironomus riparius*)	48-h Acute	Isocycloseram (TGAI Purity: 96.9%)	3.66	0.014	2	0.007	522	Yes
Freshwater midge (*Chironomus dilutes*)	60-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	3.66	0.0013 (pore water) (NOEC)	1	0.0013	2812	Yes
			3.66	0.0045[1] (pore water) (LOEC)	1	0.0045[a]	812	Yes
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	19.5	120	10	12	1.6	Yes
Marine species								
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	2.78	0.018	2	0.009	308	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	2.78	0.0042 (NOEC)	1	0.0042	661	Yes
			2.78	0.0071[2] (LOEC)	1	0.0071	391	Yes

[1] LOEC based on 39% reduction in dry weight, 16% redcution in development rate and 21% reduction in emergence; based on highest test concentration.
[2] LOEC based on 39% reduction in offspring, reduction of 27% in F0 survival and a reduction of 6.1% in F1 survival, based on highest test concentration.

Table 34 Refined level risk assessment for aquatic organisms from runoff of isocycloseram used as a foliar spray for non-orchard field crops

Organism	Exposure (applied in water unless otherwise stated)	Test substance	EEC (µg a.i./L in overlying water unless stated otherwise)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.204	0.04	2	0.02	10	Yes
Freshwater midge (*Chironomus riparius*)	48-h Acute (no sediment)	Isocycloseram Technical (Purity: 96.9%)	0.268	0.014	2	0.007	38	Yes
Freshwater midge (*Chironomus dilutes*)	60-d Chronic Spiked sediment	Isocycloseram Technical (Purity: 96.9%)	0.063	0.0013 (pore water) (NOEC)	1	0.0013	48	Yes
				0.0045[1] (pore water) (LOEC)	1	0.0045	14	Yes
			0.046 (pore water)	0.0013 (pore water) (NOEC)	1	0.0013	35	Yes
			0.046 (pore water)	0.0045[1] (pore water) (LOEC)	1	0.0045	10	Yes

Organism	Exposure (applied in water unless otherwise stated)	Test substance	EEC (µg a.i./L in overlying water unless stated otherwise)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.208	120	10	12	0.02	No
Marine species								
Estuarine amphipod *(Leptocheirus plumulosus)*	21-d Chronic Spiked sediment	Isocycloseram Technical (Purity: 96.9%)	0.046 (pore water)	0.0037 (NOEC)	1	0.0037	12	Yes
				0.0096 [2] (LOEC)	1	0.0096	4.8	Yes
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.204	0.018	2	0.009	23	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	0.125	0.0042 (NOEC)	1	0.0042	30	Yes
				0.0071[3] (LOEC)	1	0.0071	18	Yes

[1] LOEC based on 39% reduction in dry weight, 16% redcution in development rate and 21% reduction in emergence.
[2] LOEC based 41.4% reduction in survival.
[3] LOEC based on 39% reduction in offspring, reduction of 27% in F0 survival and a reduction of 6.1% in F1 survival.

Table 35 Refined level risk assessment for aquatic organisms from spray drift 1 m downwind of isocycloseram used as a foliar spray on non-orchard field crops

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.3	0.04	2	0.02	15	Yes
Freshwater midge (*Chironomus riparius*)	48-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.3	0.014	2	0.007	42	Yes
Freshwater midge (*Chironomus dilutes*)	60-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	0.3	0.0013 (pore water) (NOEC)	1	0.0013	228	Yes
			0.3	0.0045[1] (pore water) (LOEC)	1	0.0045[1] (pore water) (LOEC)	66	Yes
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	1.6	120	10	12	0.1	No
Marine species								
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.23	0.018	2	0.009	25	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	0.23	0.0042 (NOEC)	1	0.0042	54	Yes
			0.23	0.0071[2] (LOEC)	1	0.0071	32	Yes

[1] LOEC based on 39% reduction in dry weight, 16% redcution in development rate and 21% reduction in emergence.
[2] LOEC based 41.4% reduction in survival.

Table 36 Screening level risk assessment for non-target soil-dwelling terrestrial organisms (excluding birds and small wild mammals) from in-furrow application

Organism	Test substance	Exposure type	EEC (mg a.i./kg soil)	Endpoint value (mg a.i./kg soil dw)	UF	Effects metric (mg a.i./kg soil)	RQ	LOC	LOC of 1 exceeded?
Soil dwelling organisms invertebrates									
Earthworm (*Eisenia fetida*)	Isocycloseram (Purity 96.9%)	14-d Acute	0.067	> 969	2	> 484	0.0001	1	No
		56-d Chronic		10	1	10	0.01	1	No
Collembolan (*Folsomia candida*)	Isocycloseram (Purity 98.4%)	28-d $EC_{50reproduction}$	0.067	0.217	1	0.217	0.3	1	No
		28-d $NOEC_{reproduction}$	0.067	0.095	1	0.095	0.7	1	No
Predatory Mite (*Hypoaspis aculeifer*)	Isocycloseram Technical Purity: 98.4% w/w	14-d LC_{50}	0.067	0.821	2	0.41	0.2	1	No
		14-d EC_{50}	0.067	0.343	2	0.172	0.4	1	No
		14-d $NOEC_{reproduction}$	0.067	0.171	1	0.171	0.4	1	No
	SYN547950 (metabolite of isocycloseram)	14-d LC_{50}	0.053	25	2	12.5	0.004	1	No
	SYN549433 (metabolite of isocycloseram)	14-d LC_{50}	0.067	61.2	2	30.6	0.002	1	No
	SYN550918 (metabolite of isocycloseram)	14-d LC_{50}	0.055	61.2	2	30.6	0.002	1	No

Table 37 Screening level risk assessment for aquatic organisms for in-furrow applications

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Invertebrates								
Water flea (*Daphnia magna*)	48-h Acute	SYN547950 (transformation product of Isocycloseram, identified as SYN549107 in fate studies)	14.92	≥955	2	477.5	0.03	No
	48-h Acute	SYN549433 (transformation product of Isocycloseram)	14.88	≥80	2	40	0.4	No
	48-h Acute	SYN550455 (transformation product of Isocycloseram)	18.99	≥982	2	491	0.04	No
	48-h Acute	SYN550918 (transformation product of Isocycloseram, identified as SYN550738 in fate studies)	15.40	166	2	83	0.2	No
	48-h Acute	SYN551513 (transformation product of Isocycloseram, identified as	10.00	≥975	2	487.5	0.02	No

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
		SYN550603 in fate studies)						
	48-h Acute	SYN551754 (transformation product of Isocycloseram)	18.92	≥928	2	464	0.04	No
Freshwater midge (*Chironomus riparius*)	48-h Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	0.014	2	0.007	2679	Yes
	48-h Acute	SYN547950 (transformation product of Isocycloseram, identified as SYN549107 in fate studies)	14.92	51	2	25.5	0.6	No
	48-h Acute	SYN549431 (transformation product of Isocycloseram)	14.88	0.29	2	0.15	103	Yes
	48-h Acute	SYN549433 (transformation product of Isocycloseram)	18.85	161	2	80.5	0.2	No
	48-h Acute	SYN549546 (transformation product of Isocycloseram)	8.99	829	2	414.5	0.02	No
	48-h Acute	SYN550455 (transformation product of Isocycloseram)	18.99	2053	2	1026.5	0.02	No

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
	48-h Acute	SYN550918 (transformation product of Isocycloseram, identified as SYN550738 in fate studies)	15.40	0.81	2	0.41	38	Yes
	48-h Acute	SYN551113 (transformation product of Isocycloseram)	15.09	≥977	2	488.5	0.03	No
	48-h Acute	SYN551513 (transformation product of Isocycloseram, identified as SYN550603 in fate studies)	10.00	816	2	408	0.02	No
	48-h Acute	SYN551753 (transformation product of Isocycloseram, identified as SYN550737 in fate studies)	18.82	9	2	4.5	4.2	Yes
	48-h Acute	SYN551754 (transformation product of Isocycloseram)	18.92	644	2	322	0.06	No
Freshwater midge	60-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	18.75	0.0013	1	0.0013	14423	Yes

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
(*Chironomus dilutes*)								
Fish								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	120	10	12	1.6	Yes
Fathead minnow (*Pimephales promelas*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	320	10	32	0.6	No
	33-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	18.75	107	1	107	0.2	No
Vascular plants and algae								
Alga (*Navicula pelliculosa*)	96-d Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	640	2	320	0.06	No
Vascular plant Duckweed (*Lemna gibba*)	7-d Dissolved	Isocycloseram (TGAI Purity: 96.9%)	18.75	> 1100	2	> 550	<0.03	No
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	100	120	10	12	8.3	Yes
Marine species								
Invertebrates								
Crustacean Mysid shrimp	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	18.75	0.018	2	0.009	2083	Yes

Organism	Exposure	Test substance	EEC (µg a.i./L)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
(*Americamysis bahia*)	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	18.75	0.0042	1	0.0042	4464	Yes
Estuarine amphipod *(Leptocheirus plumulosus)*	21-d Chronic	Isocycloseram Technical (Purity: 96.9%)	18.75	0.0037	1	0.0037	5068	Yes
Mollusk Eastern oyster (*Crassostrea virginica*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	73	2	36.5	0.5	No
Fish								
Fish Sheepshead minnow (*Cyprinodon variegatus*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	280	10	28	0.7	No
	34-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	18.75	7.8	1	7.8	2.4	Yes
Algae								
Alga *(Skeletonema costatum*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	18.75	395	2	198	0.09	No

Table 38 Refined aquatic risk assessment for runoff of isocycloseram from in-furrow applications

Organism	Exposure (applied in water unless otherwise stated)	Test substance	EEC (µg a.i./L in overlying water unless stated otherwise)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Freshwater species								
Invertebrates								
Amphipod (*Hyalella azteca*)	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.140	0.04	2	0.02	6.8	Yes
Freshwater midge (*Chironomus riparius*)	48-h Acute (no sediment)	Isocycloseram (TGAI Purity: 96.9%)	0.171	0.014	2	0.007	24	Yes
Freshwater midge (*Chironomus dilutes*)	60-d Chronic Spiked sediment	Isocycloseram (TGAI Purity: 96.9%)	0.042	0.0013 (pore water) (NOEC)	1	0.0013	32	Yes
				0.0045[1] (pore water) (LOEC)	1	0.0045	9.3	Yes
			0.027 (pore water)	0.0013 (pore water) (NOEC)	1	0.0013	21	Yes
				0.0045[1] (pore water) (LOEC)	1	0.0045	6.0	Yes
Fish								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.140	120	10	12	0.01	No

Organism	Exposure (applied in water unless otherwise stated)	Test substance	EEC (µg a.i./L in overlying water unless stated otherwise)	Endpoint value (µg a.i./L)	UF	Effects metric (µg a.i./L)	RQ	LOC of 1 exceeded ?
Amphibians								
Rainbow trout (*Oncorhynchus mykiss)*	96-h Acute	Isocycloseram (TGAI Purity: 96.9%)	0.170	120	10	12	0.01	No
Marine species								
Invertebrates								
Crustacean Mysid shrimp (*Americamysis bahia*)	96-h Acute	Isocycloseram Technical (Purity: 96.9%)	0.140	0.018	2	0.009	16	Yes
	28-d Chronic	Isocycloseram Technical (Purity: 96.9%)	0.081	0.0042 (NOEC)	1	0.0042	19	Yes
				0.0071[2] (LOEC)	1	0.0071	11	Yes
Estuarine amphipod *(Leptocheirus plumulosus)*	21-d Chronic Spiked sediment	Isocycloseram Technical (Purity: 96.9%)	0.027 (pore water)	0.0037 (NOEC)	1	0.0037	7.3	Yes
				0.0096[3] (LOEC)	1	0.0096	2.8	Yes
Fish								
Fish Sheepshead minnow (*Cyprinodon variegatus*)	34-d Chronic	Isocycloseram (TGAI Purity: 96.9%)	0.081	7.8	1	7.8	0.01	No

[1] LOEC based on 39% reduction in dry weight, 16% reduction in development rate and 21% reduction in emergence; based on highest test concentration.
[2] LOEC based on 39% reduction in offspring, reduction of 27% in F0 survival and a reduction of 6.1% in F1 survival, based on highest test concentration.
[3] LOEC is set at the highest concentration without significant mortality (which affected ability to assess sublethal effects). Survival LOEC was 0.0096 µg a.i./L based on 41% survival.

Table 39 Screening level risk assessment for non-target terrestrial organisms (excluding birds and small wild mammals) from foliar spray in greenhouses

Organism	Test substance	Exposure type		EEC	Endpoint value	UF	Effects metric	RQ	LOC	LOC of 0.4, 1 or 2 exceeded?
Invertebrates										
Bee	Isocycloseram (Purity 96.9%)	72-h adult acute oral		4.301 µg a.i./bee	0.28 µg a.i./bee	1	0.28 µg a.i./bee	15.4	0.4	Yes
		96-h adult acute contact		0.361 µg a.i./bee	0.26 µg a.i./bee	1	0.26 µg a.i./bee	1.4	0.4	Yes
		10-d adult chronic		14.729 mg a.i./kg diet	0.11 mg a.i./kg diet	1	0.11 mg a.i./kg diet	134	1	Yes
		72-h larval single exposure		14.729 mg a.i./kg diet	3.88 mg a.i./kg diet	1	3.88 mg a.i./kg diet	3.8	0.4	Yes
		22-d larval repeated exposure		14.729 mg a.i./kg diet	0.10 mg a.i./kg diet	1	0.1 mg a.i./kg diet	147	1	Yes
	SYN549106 (metabolite of isocycloseram)	96-h adult acute oral		3.398 µg a.i./bee	0.18 µg a.i./bee	1	0.18 µg a.i./bee	19	0.4	Yes
		96-h adult acute contact		0.285 µg a.i./bee	0.072 µg a.i./bee	1	0.072 µg a.i./bee	4.0	0.4	Yes
Predatory arthropod *(Typhlodromus pyri)*	SYN547407 DC 100 formulated product (100 g a.i./L isocycloseram)	7-d LR_{50} Contact (glass plate)	On-field greenhouse	168.584 g a.i./ha	0.0059 g a.i./ha	1	0.0059 g a.i./ha	28574	2	Yes
Parasitoid wasp (*Aphidius rhopalosiphi*)	SYN547407 DC 100 (Formulated product) Purity: 9.29% w/w	48-h LR_{50} Contact (glass plate)	On-field greenhouse	168.584 g a.i./ha	0.42 g a.i./ha	1	0.42 g a.i./ha	401	2	Yes

Table 40 Refined risk assessment for non-target terrestrial organisms (excluding birds, small wild mammals and bees) from foliar spray in greenhouses

Organism	Test substance	Exposure type		EEC (g a.i./ha)	Endpoint value	UF	Effects metric (g a.i./ha)	RQ	LOC of 1 exceeded?
Invertebrates									
Predatory arthropod *(Typhlodromus pyri)*	SYN547407 DC 100 formulated product (100 g a.i./L isocycloseram)	7-d LR_{50} Contact (Dried residues on foliage)	In-greenhouse (on-field) 80% foliar deposition	128.7	0.0072 g a.i./ha	1	0.0072	17875	Yes
		14-d reproduction ER_{50} Contact (Dried residues on foliage)		128.7	0.006 g a.i./ha	1	0.006	21450	Yes
Parasitoid wasp (*Aphidius rhopalosiphi*)	SYN547407 DC 100 formulated product (100 g a.i./L isocycloseram)	48-h LR_{50} Contact (Dried residues on foliage) (13 day study)	In-greenhouse (on-field) 80% foliar deposition	128.7	2.46 g a.i./ha	1	2.46	52	Yes
		13-d reproduction ER_{50}: > 2.44[1]		128.7	> 2.44 g a..i./ha	1	> 2.44	53	Yes

[1] A 13-day $ER_{50\ reproduction}$ could not be determined due to high adult mortality in the test vessels above 2.44 g a.i./ha.

Table 41 Supported uses for A21377 CP and A21708 CP

All supported uses are for control of the listed pest(s) with a maximum of two foliar applications per year with a minimum re-treatment interval of 7 days at rates up to 20 g a.i./ha or a single application per year at 30 g a.i./ha, using conventional ground or airblast equipment only.

Crop(s)	Pest(s)	Application rate(s)		
		A21377 CP (mL/ha)	A21708 CP (mL/ha)	Active ingredient (g a.i./ha) (either product)
Potato	Colorado potato beetle	50-100	100-200	10-20
Tuberous and Corm Vegetables (Crop Subgroup 1C)	Potato leafhopper	100-150	200-300	20-30
	European corn borer (suppression)	150	300	30
Leafy Vegetables (Crop Group 4-13), except head lettuce	Potato leafhopper, cabbage looper	100-150	200-300	20-30
Brassica Leafy Greens (Crop Subgroup 4-13B)	Flea beetles, imported cabbageworm, diamondback moth	100-150	200-300	20-30
Brassica Head and Stem Vegetables (Crop Group 5-13)	Flea beetles, cabbage looper, imported cabbageworm, diamondback moth	100-150	200-300	20-30
Fruiting Vegetables (Crop Group 8-09)	Colorado potato beetle	50-100	100-200	10-20
	Potato leafhopper, broad mite, two-spotted spider mite, cabbage looper	100-150	200-300	20-30
	European corn borer (suppression)	150	300	30
Cucurbit Vegetables (Crop Group 9)	Two-spotted spider mite	100-150	200-300	20-30
	Squash bug	150	300	30

Crop(s)	Pest(s)	Application rate(s)		
		A21377 CP (mL/ha)	A21708 CP (mL/ha)	Active ingredient (g a.i./ha) (either product)
Pome Fruits (Crop Group 11-09)	European red mite, two-spotted spider mite	100-150	200-300	20-30
Stone Fruits (Crop Group 12-09)	European red mite, two-spotted spider mite	100-150	200-300	20-30
Tree Nuts (Crop Group 14-11)	Two-spotted spider mite	100-150	200-300	20-30
Corn (field, seed and pop) (A21708 CP only)	Two-spotted spider mite	100-150	200-300	20-30
Soybean	Two-spotted spider mite, bean leaf beetle	100-150	200-300	20-03
	Brown stink bug, green stink bug	150	300	30
Peanut	Potato leafhopper, two-spotted spider mite	100-150	200-300	20-30

Table 42 Supported uses for A23294 TO

For turf and sod, apply as a foliar spray, with a maximum of 1 application per year. Apply in a spray volume of 200 to 1600 L/ha.
For greenhouse ornamentals, apply as a foliar spray with a minimum reapplication interval of 7 to 14 days, depending on the pest.

Crop(s)	Pest(s)	Application Rate(s)	
		Product (mL/ha or mL/100 L	Active ingredient (g a.i./ha or g a.i./100 L
Turf and Sod	Annual bluegrass weevil (suppression), billbugs, and turf caterpillars (fall armyworm, black cutworm, sod webworm)	555 mL/ha	50 g/ha ICS 61 g/ha JIY

Crop(s)	Pest(s)	Application Rate(s)	
		Product (mL/ha or mL/100 L	Active ingredient (g a.i./ha or g a.i./100 L
Greenhouse Ornamentals (including cut flowers)	Cabbage looper	50 mL/100 L	4.5 g/100 L ICS 5.5 g/100 L JIY
	Japanese beetle adults (suppression)	100-114 mL/100 L	9-10.3 g/100 L ICS 11-12.5 g/100 L JIY
	Obliquebanded leafroller, threelined leafroller, variegated leafroller, eyespotted budmoth, redbanded leafroller, tufted apple budmoth	50-100 mL/100 L	4.5-9 g/100 L ICS 5.5-11 g/100 L JIY
	Dipteran leafminers (*Liriomyza sativae, Liriomyza trifolii)*, green fruitworm	50-75 mL/100 L	4.5-6.75 g/100L ICS 5.5-8.25 g/100L JIY
	Mites, thrips	57-114 mL/100 L	5.1-10.3 g/100 L ICS 6.3-12.5 g/100 L JIY
	Dogwood borer	75-100 mL/100 L	6.75-9 g/100 L ICS 8.25-11 g/100 L JIY
Greenhouse Ornamentals (Brassica only)	Imported cabbageworm, diamondback moth, swede midge	50 mL/100 L	4.5 g/100 L ICS 5.5 g/100 L JIY
Greenhouse Ornamentals (non-bearing pome and stone fruit trees only)	Western tentiform leafminer	50-75 mL/100 L	4.5-6.75 g/100L ICS 5.5-8.25 g/100L JIY
	White apple leafhopper (suppression)	75-100 mL/100 L	6.75-9 g/100 L ICS 8.25-11 g/100 L JIY
Greenhouse Ornamentals (non-bearing pome fruit trees only)	Spotted tentiform leafminers, European apple sawfly	50-75 mL/100 L	4.5-6.75 g/100L ICS 5.5-8.25 g/100L JIY
Greenhouse Ornamentals (*Viburnum* spp. only)	Viburnum leaf beetle	57-114 mL/100L	5.1-10.3 g/100 L ICS 6.3-12.5 g/100 L JIY
Greenhouse Ornamentals (non-bearing stone fruit	Peach twig borer	75-100 mL/100L	6.75-9 g/100 L ICS 8.25-11 g/100 L JIY

Crop(s)	Pest(s)	Application Rate(s)	
		Product (mL/ha or mL/100 L	Active ingredient (g a.i./ha or g a.i./100 L
trees and *Prunus* spp. only)			

ICS = isocycloseram
JIY = chlorantraniliprole

Table 43 Supported uses for EQUENTO RFC

For lentils: For in-season stand establishment and wireworm mortality, use the low rate for light to moderate wireworm populations. For fields with a history of wireworms and under high wireworm infestations, use the high rate.

Crop(s)	Pest(s)	Application rate(s)	
		Product (mL/per 100 kg seed)	Active ingredient (g a.i./100 kg seed
Lentils	Wireworms	6.25-12.5	2.5-5.0

Table 44 Supported uses for A22466 CP

Apply at planting in-furrow in a minimum of 20 L water per hectare.

Crop(s)	Pest(s)	Application Rate(s)	
		Product (mL/ 100 m row)	Active ingredient (g a.i./100 m row)
Corn (field, seed, pop)	Corn rootworm larvae (northern, western) and wireworms	1.84-3.78	0.55-1.13

Appendix II Supplemental maximum residue limit information—International situation and trade implications

Isocycloseram is an active ingredient that is concurrently being registered in Canada and the United States for use on several crops.

Table 1 compares the MRLs proposed for isocycloseram in Canada with corresponding American tolerances and Codex MRLs.[5] American tolerances will be listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide, once adopted. A listing of established Codex MRLs is available on the Codex Alimentarius Pesticide Index webpage, by pesticide or commodity.

Table 1 Comparison of Proposed Canadian MRLs, American Tolerances and Codex MRLs

Commodity	Proposed Canadian MRLs (ppm)	Established US Tolerances (ppm)	Established Codex MRLs (ppm)
Leafy vegetables (crop group 4-13), except head lettuce	10	10	Not established
Brassica Head and Stem vegetable (crop group 5-13)	4.0	4	0.7 (Broccoli) 2.0 (Brussels sprouts) 4 (Cabbages, head) 0.5 (Cauliflower)
Dried tomatoes	2.0	2	2
Dried prune plums	1.5	1.5	1.5
Stone fruits (crop group 12-09)	1.0	1	1 (Cherries subgroup) 0.3 (Peaches (including apricots and nectarines) subgroup) 0.4 (Plums (including fresh prunes) subgroup)
Fruiting vegetables (crop group 8-09)	0.6	0.6	0.3 (Eggplant) 0.6 (Peppers chili) 4.2 (Peppers chili, dried) 0.3 (Peppers, sweet (including pimento or pimiento)) 0.5 (Tomato)
Almond oil	0.5	Not established	Not established
Pome fruits (crop group 11-09)	0.4	0.4	0.4

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

Commodity	Proposed Canadian MRLs (ppm)	Established US Tolerances (ppm)	Established Codex MRLs (ppm)
Tree nuts (crop group 14-11)	0.2	0.2 (almond; almond, tropical; beechnut; bunya; candlenut; chestnut; chinquapin; gingko; nut, monkey puzzle; nut, okari; nut, peach palm; nut, pili; nut, pine; pequi; pine, Brazilian; pistachio; yellowhorn) 0.01 (African nut-tree; bur oak; butternut; cashew; chestnut, Guiana; coconut; hazelnut; heartnut; horse-chestnut, Japanese; monkey-pot; nut, Brazil; nut, cajou; nut, coquito; nut, dika; nut, hickory; nut, macadamia; nut, mongongo; nut, pachira; nut, sapucaia; pecan; walnut, black; walnut, English)	Not established
Cucurbit vegetables (crop group 9)	0.15	0.15	0.1 (Cucumber) 0.15 (Melons, except watermelon) 0.09 (Summer squash)
Dry soybeans	0.15	0.15	0.15
Tuberous and corm vegetables (crop subgroup 1C)	0.01	0.01	0.01 (Potato)
Lentils, dry	0.01	0.01 (Vegetable, legume, pulse, bean, dried shelled, except soybean (crop subgroup 6-22E); Vegetable, legume, pulse, pea, dried shelled (crop subgroup 6-22F))	Not established
Peanuts	0.01	0.01	Not established
Head lettuce	0.01	10 ppm (Vegetable, leafy; crop group 4-16)	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.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

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3245913	2021, Isocycloseram (SYN547407) Document M-II, Section 2 - Analytical Methods, DACO: 12.7,2.13.1,2.13.4,2.15,2.16,5.10,7.2.1,7.2.2,7.2.3,7.2.4,7.2.5, 8.2.2.1,8.2.2.2,8.2.2.3,8.2.2.4,8.6,Document M,IIA 4.1.1,IIA 4.1.2,IIA 4.1.3,IIA 4.1.4,IIA 4.2.1,IIA 4.2.2,IIA 4.2.3,IIA 4.2.4,IIA 4.2.5,IIA 4.2.6,IIA 4.2.7,IIA 4.3,IIA 4.4,IIA 4.5,IIA 4.6,IIA 4.7,IIA 4.8,IIA 4.9
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3245973 2018, SYN547407 - Validation of the Analytical Method for the Determination of the Test Substance in Pollen and Nectar, DACO: 2.16,8.6,IIA 4.9

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2.0 Human and Animal Health

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3246943 2021, Chlorantraniliprole/Isocycloseram SC (A23294D) - Acute Inhalation Toxicity in Rats, DACO: 4.6.3,IIIA 7.1.3

3246944 2020, Chlorantraniliprole/Isocycloseram SC (A23294D) - Primary Skin Irritation in Rabbits, DACO: 4.6.5,IIIA 7.1.4

3246945 2020, Chlorantraniliprole/Isocycloseram SC (A23294D) - In Vitro Skin Irritation Test in the EpiDerm^{TM} Model (EPI-200-SIT), DACO: 4.6.5,IIIA 7.1.4

3246946 2020, Chlorantraniliprole/Isocycloseram SC (A23294D) - Primary Eye Irritation in Rabbits, DACO: 4.6.4,IIIA 7.1.5

3246947 2020, Chlorantraniliprole/Isocycloseram SC (A23294D) - In Vitro Eye Irritation Test in Isolated Chicken Eyes, DACO: 4.6.4,IIIA 7.1.5

3246948 2020, Chlorantraniliprole/Isocycloseram SC (A23294D) - Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6,IIIA 7.1.6

3246058 2019, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Representative Raw Agricultural Commodities of the Pome Fruits Crop Group (11-09) - Canada 2017, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246059 2020, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Cherry, Peach, and Plum as Representative Commodities of Stone Fruits, Crop Group (12-09) Canada 2017, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246061 2021, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Pecan and Almond Raw Agricultural and Processed Commodities as Representative Crops of the Tree Nuts Crop Group (14-12), USA 2018, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246062 2020, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Potato as a Representative Crop of Tuberous and Corm Vegetables, Subgroup 1C - Canada 2017, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246063 2020, SYN547407 DC (A21708F) - Magnitude of the Residue in or on Head Lettuce, Leaf Lettuce, Spinach, and Mustard Greens as Representative Crops of the Leafy Vegetable Group, (Crop Group 4-16) USA 2017, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246064 2020, SYN547407 DC (A21708F) - Magnitude of the Residue in or on Cabbage, Broccoli, Cauliflower, and Brussels Sprouts as Representative Crops of Brassica Head and Stem Vegetables Crop Group 5-16 USA 2017, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246065 2020, SYN547407 DC (A21708F) and SYN547407 SC (A21377X) - Magnitude of the Residues in or on Melon, Cucumber, and Summer Squash as Representative Crops of Cucurbit Vegetables Crop Group CG9 Following Foliar Application USA, 2018, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246067 2020, SYN547407 FS (A22241C) - Magnitude of the Residues in or on Dry Bean as a Representative Crop of Legume Vegetables Subgroup 6C (CSG6C) Following Seed Treatment, USA 2018, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246068 2020, SYN547407 FS (A22241C) - Magnitude of the Residues in or on Dry Pea as a Representative Crop of Legume Vegetables Subgroup 6C (CSG6C) Following Seed Treatment, Canada 2018, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1

3246072 2019, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Cherry, Peach, and Plum as Representative Commodities of Stone Fruits, Crop Group 12-12 - USA 2017, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4

3246073 2021, SYN547407 DC (A21708F) - Magnitude of the Residue in or on Processed Commodities of Peaches USA 2019, DACO: 7.4.1,7.4.2,7.4.5,7.4.6, IIA 6.3.1,IIA 6.5.3,IIA 6.5.4

3246074 2020, ISM-555 - Magnitude of the Residue on Peanut, DACO: 7.4.1,7.4.2,7.4.5, 7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4

3246075	2020, SYN547407 DC (A21708F) and SYN547407 SC (A21377X) - Magnitude of the Residues in or on Fruiting Vegetables (Bell/Non-Bell Pepper, Eggplant and Tomato) as Representative Crops of Fruiting Vegetables Subgroup CG8-09 and Tomato Processed Commodities Following Foliar Application USA, 2018, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246080	2019, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Potato as a Representative Crop of Tuberous and Corm Vegetables, Subgroup 1C - USA 2017, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.2,IIA 6.5.3,IIA 6.5.4
3246081	2020, SYN547407 SC (A21550J) and SYN547407 DC (A21708F) - Magnitude of the Residues in or on Representative Raw Agricultural and Processed Commodities of Field Corn and Popcorn - United States 2017, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246082	2021, SYN547407 DC (A21708F) - Magnitude of the Residue in or on Tomato Processed Commodities USA 2019, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246083	2021, SYN547407 DC (A21708F) - Magnitude of the Residue in or on Processed Commodities of Apples USA 2019, DACO: 7.4.1,7.4.2,7.4.5,7.4.6, IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246084	2021, SYN547407 DC (A21708F) - Magnitude of the Residue in Soybean Processed Commodities USA 2019, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246085	2021, SYN547407 DC (A21708F) - Magnitude of the Residue in or on Spinach Processed Commodities USA 2019, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246089	2020, SYN547407 SC (A21550L) and SYN547407 DC (A21708F) - Magnitude of Residues in or on Soybeans, USA 2017, DACO: 7.4.1,7.4.2,7.4.5,7.4.6, IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246090	2019, SYN547407 DC (A21708F) - Magnitude of the Residues in or on Apples and Pears as Representative Crops of the Pome Fruits Crop Group, (11-10) - USA 2017, DACO: 7.4.1,7.4.2,7.4.5,7.4.6,IIA 6.3.1,IIA 6.5.3,IIA 6.5.4
3246034	2019, SYN547407 SC (A21377X) - The In Vitro Percutaneous Absorption of Radiolabelled SYN547407 in Concentrate Formulation and Three In-Use Dilutions Through Rat Split-Thickness Skin, DACO: 5.8,IIA 5.9.9
3246035	2019, SYN547407 SC (A21377X) - The In Vitro Percutaneous Absorption of Radiolabelled SYN547407 in Concentrate Formulation and Three In-Use Dilutions Through Human Split-Thickness Skin, DACO: 5.8,IIA 5.9.9
3246036	2019, SYN547407 SC (A21377X) - The In Vivo Percutaneous Absorption of [14C]-SYN547407 in Concentrate Formulation and Three In-Use Dilutions in the Rat, DACO: 5.8,IIA 5.9.9

3246037 2021, Isocycloseram SC (A21550L) - The In Vitro Percutaneous Absorption of Radiolabelled Isocycloseram in a Concentrate Formulation and Two In-Use Dilutions Through Human Split-Thickness Skin, DACO: 5.8,IIA 5.9.9

3246038 2020, SYN547407 DC (A21708E) - The In Vitro Percutaneous Absorption of Radiolabelled SYN547407 in Concentrate Formulation and Three In-Use Dilutions Through Human Split-Thickness Skin, DACO: 5.8,IIA 5.9.9

3246669 2021, Isocycloseram (SYN547407) - Laboratory Dust Off Measurements of Cereal, Canola and Lentil Seeds Treated with A22241 ST, A22725 ST and A23128 ST and Bridging to Exposure Data, DACO: 5.14,IIIA 7.11

3283874 2021, Isocycloseram A21377 CP (A21377X) Document M-III, Section 3 - Amendment 1 (Replaces MRID Number 51228714) Toxicological Studies, DACO: 12.7.4,12.7.5,Document M,Document N

3290041 2021, Isocycloseram A21708 CP (A21708G) Document M-III, Section 3 - Toxicological Studies (Replaces MRID Number 51228611), DACO: 12.7.4,12.7.5,Document M,Document N

3245981 2020, SYN547407 SC (A21377X) Dissipation of Dislodgeable Foliar Residues in Apples, USA 2018, DACO: 5.9(A)

3245982 2020, SYN547407 SC (A21377X) - Dissipation of Dislodgeable Foliar Residues in Tomatoes, USA 2018, DACO: 5.9(A)

3390405 2020, Supplemental Data to Support - SYN547407 SC (A21377X) - Determination of Transferable Turf Residues, USA 2019, DACO: 5.9B

3245983 2021, Isocycloseram (SYN547407) - Rationale to Support a Request to Waive Series 875 Data Requirements, DACO: 5.3,5.4,5.6,5.9(C).

3.0 Environment

PMRA Document Number	Reference
3245949	2020, SYN547407 - Analytical Method GRM072.16A for the Determination of Anaerobic Metabolites SYN548569, SYN549110, SYN549433, SYN549543. SYN549546, SYN550321, SYN550455, SYN550602, SYN550603, SYN551057, SYN551113 and SYN551248 in Soil, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6
3245950	2021, SYN547407 - Independent Laboratory Validation of Residue Method (GRM072.16A) for the Determination of Anaerobic Metabolites SYN548569, SYN549110, SYN549433, SYN549543, SYN549546, SYN550321, SYN550455, SYN550602, SYN550603, SYN551057, SYN551113, and SYN551248 in Soil by LC-MS/MS, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6

3245951 2021, SYN547407 - Independent Laboratory Validation of Residue Method (GRM072.12A) for the Determination of SYN547407 and its Metabolites SYN549107, SYN549431, and SYN550738 in Soil by LC-MS/MS, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6

3245952 2019, SYN547407 - Validation of Analytical Method GRM072.12A for the Determination of SYN547407 and its Metabolites SYN549107, SYN549431 and SYN550738 in Soil, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6

3245953 2020, SYN547407 - Analytical Method GRM072.12A for the Determination of SYN547407 and its Metabolites SYN549107, SYN549431 and SYN550738 in Soil, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6

3245954 2021, SYN547407 - Residue Method GRM072.17A for the Determination of SYN547407 and Metabolites SYN549107, SYN549431, SYN550455 and SYN551485 in Water Includes Validation Data, DACO: 8.2.2.3,IIA 4.5

3245955 2021, SYN547407 - Independent Laboratory Validation of Residue Method GRM072.17A for the Determination of SYN547407 and Metabolites SYN549107, SYN549431, SYN550455 and SYN551485 in Water, DACO: 8.2.2.3,IIA 4.5

3245972 2021, SYN547407 - Analytical Method GRM072.05A for the Determination of SYN547407 in Pollen and Nectar, DACO: 2.16,8.6,IIA 4.9

3245973 2018, SYN547407 - Validation of the Analytical Method for the Determination of the Test Substance in Pollen and Nectar, DACO: 2.16,8.6,IIA 4.9

3246095 2019, SYN547407 - Aerobic Soil Metabolism of [14C]-SYN547407, DACO: 8.2.3.4.2,IIA 7.1.1

3246096 2019, SYN547407 - Anaerobic Soil Metabolism of 14C-SYN547407, DACO: 8.2.3.4.4,IIA 7.1.2

3246098 2019, SYN547407 - Soil Photolysis of [14C]-SYN547407, DACO: 8.2.3.3.1,IIA 7.1.3

3246100 2021, SYN549107 - Rate of Degradation of [14C]-SYN549107 in Aerobic Soil, DACO: 8.2.3.4.2,IIA 7.2.3

3246101 2021, SYN550738 - Rate of Degradation of [14C]-SYN550738 in Aerobic Soil, DACO: 8.2.3.4.2,IIA 7.2.3

3246102 2021, SYN547407 SC (A21550L) - Dissipation Trial to Determine Persistence and Leaching Movement of SYN547407 and any Significant Soil Degradates in Soil, DACO: 8.3.2,IIA 7.3.1

3246104 2021, SYN547407 (A21550L) - Dissipation of Insecticide SYN547407 SC (400) In Soil When Applied to Turf and Bare Soil in New York, USA, DACO: 8.3.2,IIA 7.3.1

3246109 2021, SYN547407 (A21550L) - Dissipation of Insecticide SYN547407 SC (400) In Soil When Applied to Bare Soil in New York, USA, DACO: 8.3.2,IIA 7.3.1

3246114	2021, SYN547407 - Dissipation Trial to Determine Persistence and Leaching Movement of SYN547407 and Any Significant Soil Degradates in Soil, DACO: 8.3.2,IIA 7.3.1
3246116	2021, Freezer Stability of SYN547407 and Degradation Products in Representative Turfgrass Clippings, Thatch-Sod Layer, and Soil Matrices Under Freezer Storage Conditions, DACO: 8.3.2,IIA 7.3.1
3246117	2019, SYN547407 - Adsorption/Desorption of [14C]-SYN547407 in Six Soils, DACO: 8.2.4.2,IIA 7.4.1
3246118	2020, SYN547407 - Adsorption/Desorption of 14C-SYN547407 in Three Soils, DACO: 8.2.4.2,IIA 7.4.1
3246119	2021, SYN549107 - Adsorption and Desorption of [14C]-SYN549107 in Six Soils, DACO: 8.2.4.2,IIA 7.4.2
3246120	2021, SYN550738 - Adsorption and Desorption of [14C]-SYN550738 in Six Soils, DACO: 8.2.4.2,IIA 7.4.2
3246121	2019, SYN547407 - Hydrolysis of 14C-SYN547407, DACO: 8.2.3.2,IIA 2.9.1,IIA 7.5
3246122	2019, SYN547407 - Photolysis of 14C-SYN547407 in pH 4 Buffer Solution, DACO: 8.2.3.3.2,IIA 2.9.2,IIA 7.6
3246124	2019, SYN547407 - Aerobic Aquatic-Sediment Metabolism of 14C-SYN547407, DACO: 8.2.3.6,IIA 7.8.3
3246125	2019, SYN547407 - Anaerobic Aquatic-Sediment Metabolism of 14C-SYN547407, DACO: 8.2.3.6,IIA 7.8.3
3246126	2021, SYN547407 - Anaerobic Aquatic-Sediment Metabolism of 14C-SYN547407, DACO: 8.2.3.6,IIA 7.8.3
3246127	2021, SYN547407 - Metabolism of 14C-SYN547407 in One Aerobic Aquatic-Sediment System, DACO: 8.2.3.6,IIA 7.8.3
3246128	2016, SYN547407 - An Acute Oral Toxicity Study with the Northern Bobwhite Using a Sequential Testing Procedure, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
3246129	2018, SYN547407 - An Acute Oral Toxicity Study with the Canary Using a Sequential Testing Procedure, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
3246130	2016, SYN547407 - An Acute Oral Toxicity Study with the Mallard Using a Sequential Testing Procedure, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
3246131	2017, SYN547407 - A Dietary LC50 Study with the Northern Bobwhite, DACO: 9.6.2.4,9.6.2.5,IIA 8.1.2
3246132	2017, SYN547407 - A Dietary LC50 Study with the Mallard, DACO: 9.6.2.6,IIA 8.1.3
3246133	2018, SYN547407 - A Reproduction Study with the Northern Bobwhite, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4

3246134 2018, SYN547407 - A Reproduction Study with the Mallard, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4

3246137 2019, SYN547407 - Acute Toxicity to Mysids (Americamysis bahia) Under Static-Renewal Conditions, DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

3246138 2019, SYN547407 - Life-Cycle Toxicity Test with Mysids (Americamysis bahia), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

3246139 2018, SYN547407 - Acute Toxicity Test with Eastern Oyster (Crassostrea virginica) Under Flow Through Conditions, DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

3246140 2020, SYN547407 - Acute Toxicity to Sheepshead Minnow (Cyprinodon variegatus) Under Flow Through Conditions, DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1

3246141 2018, SYN547407 - 96-Hour Toxicity Test with the Marine Diatom, Skeletonema costatum, DACO: 9.5.2.4.1,IIA 8.11.2

3246142 2018, SYN547407 - Early Life-Stage Toxicity Test with Sheepshead Minnow (Cyprinodon variegatus), DACO: 9.5.2.4.1,IIA 8.11.2

3246143 2019, SYN547407 SC (A21550L) - Evaluation of the Phytotoxicity to Non Target Terrestrial Plant Seedling Emergence and Seedling Growth Test, DACO: 9.8.4,IIA 8.12

3246144 2019, SYN547407 SC (A21550L) - Evaluation of the Phytotoxicity to Non Target Terrestrial Plant Vegetative Vigour Test, DACO: 9.8.4,IIA 8.12

3246146 2016, A20792A - A Semi-Field Study to Evaluate Side Effects on Honeybees (Apis mellifera L.) in Soybean in Brazil 2014 / 2015, DACO: 9.6.6,9.9,IIA 8.16.2

3246147 2020, SYN547407 SC 400 (A21550L) - A Semi-Field Study to Evaluate Side Effects on Honeybees (Apis mellifera L.) in Cotton in Brazil 2019, DACO: 9.6.6,9.9,IIA 8.16.2

3246148 2021, SYN547407 SC (400) (A21550L) - A Semi-Field Study to Evaluate Side Effects on Honeybees (Apis mellifera L.) in Cotton (Gossypium hirsutum) in the US 2019, DACO: 9.6.6,9.9,IIA 8.16.2

3246149 2020, SYN547407 SC 400 (A21550L) A Semi-Field Study to Evaluate Side Effects on Honeybees (Apis mellifera L.) in Niger in Brazil 2019, DACO: 9.6.6,9.9,IIA 8.16.2

3246150 2020, SYN547407 (A21708F) - Assessment of Potential Side Effects on the Honey Bee (Apis mellifera L.) in a Semi-Field Study After Application to Flowering Buckwheat (Fagopyrum esculentum), DACO: 9.6.6,9.9,IIA 8.16.2

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3246152 2019, SYN547407 (A21708F) - Assessment of Potential Side Effects on the Honey Bee (Apis mellifera L.) in a Semi-Field Study after Application to Flowering Buckwheat (Fagopyrum esculentum), DACO: 9.6.6,9.9,IIA 8.16.2

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3246154 2020, SYN547407 (A21377X): Effects on Honeybee (Apis mellifera L.) Adults and Brood in Semi-Field Test Conditions with soybean in Brazil, DACO: 9.6.6,9.9,IIA 8.16.2

3246155 2018, SYN547407 - Acute Toxicity to Rainbow Trout (Oncorhynchus mykiss) Under Flow-Through Conditions, DACO: 9.5.2.1,9.5.2.3,IIA 8.2.1.1

3246156 2021, SYN547407 - Acute Toxicity to Carp (Cyprinus carpio) Under Flow Through Conditions, DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2

3246157 2018, SYN547407 - Acute Toxicity to Fathead Minnow (Pimephales promelas) Under Flow Through Conditions, DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2

3246158 2018, SYN547407 - Early Life-Stage Toxicity Test with Fathead Minnow (Pimephales promelas), DACO: 9.5.3.1,IIA 8.2.4

3246159 2020, [14C]SYN547407 - Bioaccumulation in Bluegill Sunfish (Lepomis macrochirus): Aqueous Exposure, DACO: 9.4.8,9.5.6,IIA 8.2.6.1,IIA 8.2.7

3246160 2018, SYN547407 - Acute Toxicity to Water Fleas (Daphnia magna) Under Static Conditions, DACO: 9.3.2,IIA 8.3.1.1

3246161 2021, SYN547950 - Effects on Daphnia magna in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1

3246162 2021, SYN549433 - Effects on Daphnia magna in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1

3246163 2021, SYN550455 - Effect on Daphnia magna in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1

3246164 2021, SYN550918 - Effects on Daphnia magna in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1

3246165 2021, SYN551513 - Effects on Daphnia magna in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1

3246166 2021, SYN551754 - Effects on Daphnia magna in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1

3246168 2020, SYN547407 - Acute Toxicity to Caddisflies (Pycnopsyche gentilis) Under Static Conditions, DACO: 9.3.4,IIA 8.3.1.2

3246169 2021, SYN547407 - Acute Toxicity to Mayflies (Hexagenia limbata) Under Static Conditions, DACO: 9.3.4,IIA 8.3.1.2

3246170 2019, SYN547407 - Acute Toxicity to Midge (Chironomus riparius) Under Static Conditions, DACO: 9.3.4,IIA 8.3.1.2

3246171 2021, SYN547950 - Effect on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246172 2021, SYN549431 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246173 2021, SYN549433 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246174 2021, SYN549546 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246175 2021, SYN550455 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246176 2021, SYN550918 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246177 2021, SYN551113 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246178 2021, SYN551513 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246179 2021, SYN551753 - Effects on the First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246180 2021, SYN551754 - Effects on First-Instar Larvae of Chironomus riparius in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2

3246181 2021, SYN547407 - Acute Toxicity to Freshwater Rotifers (Brachionus calyciflorus) Under Static Conditions, DACO: 9.3.4,IIA 8.3.1.3

3246182 2021, SYN547407 - Acute Toxicity to the Water Louse (Caecidotea communis) Under Static-Renewal Conditions, DACO: 9.3.4,IIA 8.3.1.3

3246183 2021, SYN547407 - Acute Toxicity to the Grass Shrimp (Palaemonetes paludosus) Under Static-Renewal Conditions, DACO: 9.3.4,IIA 8.3.1.3

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4.0 Value

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3246545 2021, ISM-555 CP NA 2019 DC100/SC200 profiling- ICW/CL in brassica, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246547 2019, ISM-555 CP NA 2019 DC100/SC200 profiling- May spray for mites in tree nuts, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246552 2019, Phytotoxicity and efficacy of Isocycloseram as foliar application against red spider mites (RSM) on maize in South Africa, DACO: 10.2.3.3,10.2.3.4, IIIA 6.1.2,IIIA 6.1.3

3246693 2021, Efficacy Summary Table - A22466 CP, DACO: 10.2.3.3,10.2.3.4,10.3.2,12.7,Document M,IIIA 6.1.2,IIIA 6.1.3,IIIA 6.2.1

3246697 2021, 3-31-2021 DER - A22466 CP (A22466 G) Data Evaluation Record, DACO: 10.6,3.7,IIIA 1.7,IIIA 2.15 CBI

3246698 2020, ISM-555: 2020 US SAI in corn for corn rootworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246699 2020, ISM-555: 2020 US SAI in corn for corn rootworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246700 2021, ISM-555 CP NA 2019 formulation development for soil uses - wireworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246701 2021, ISM-555 CP NA 2019 formulation development for soil uses - grubs in corn, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246702 2021, ISM-555 CP NA 2019 formulation development for soil uses - corn rootworm in corn, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246703 2019, ISM-555 CP NA 2019 formulation development for soil uses - corn rootworm in corn, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246704 2019, ISM-555 CP NA 2019 formulation development for soil uses - corn rootworm in corn, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246705 2018, ISM-555 CP NA 2018 formulation development for soil uses - wireworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246706 2016, SYN547407 Formulations for Corn Rootworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246707 2020, ISM-555: 2020 US SAI in corn for corn rootworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246708 2021, ISM-555 CP NA 2019 formulation development for soil uses - wireworm, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246709 2019, ISM-555 CP NA 2019 formulation development for soil uses - corn rootworm in corn, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246738 2021, Isocycloseram A22725 ST (A22725F) - Document M-III, Section 7 - Efficacy Data and Information - Canada, DACO: 10.2.3.3,10.2.3.4,10.3.2,12.7,Document M,IIIA 6.1.2,IIIA 6.1.3,IIIA 6.2.1

3246744 2021, A22725 ST - Efficacy Summary Table, DACO: 10.2.3.3,10.2.3.4,10.3.2,12.7,Document M,IIIA 6.1.2,IIIA 6.1.3,IIIA 6.2.1

3246754 2021, DER - A22725 ST (A22725F) Data Evaluation Record, DACO: 10.6,3.7,IIIA 1.7,IIIA 2.15 CBI

3246755 2021, Determine LER of Isocycloseram (A22241A) for control of wireworms in lentils, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246756 2021, Determine LER of Isocycloseram (A22241A) for control of wireworms in lentils, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246757 2021, Determine LER of Isocycloseram Solo Formulation for control of wireworms in Pulses, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246759 2021, Determine LER of Isocycloseram Solo Formulation for control of wireworms in Lentils, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246760 2021, Compare Plinazolin 100FS and 400FS formulations for equivalency for control of wireworms in lentils, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246767 2021, Compare Plinazolin 100FS and 400FS formulations for equivalency for control of wireworms in lentils, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246858 2021, DER - Atexzo Duo (A23294D) Data Evaluation Record, DACO: 10.6,3.7,IIIA 1.7,IIIA 2.15 CBI

3246859 2020, Evaluate ISM-555 for control of grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246860 2020, Evaluate ISM-555 for control of grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246862 2017, ISM-555: Evaluation of formulations for control of annual white grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246863 2019, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding pests, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246864 2021, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246865 2017, ISM-555: Evaluate A21708C and A21377W for control of billbugs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246866 2015, SYN547407: White grub complex in turf (Preventative), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246867 2021, ISM-555: Greenhouse evaluation of foliar applications - non-Tetranychus mites, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246868 2021, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding pests, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

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3246870 2017, ISM-555: Evaluation of formulations for control of annual white grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246871 2016, SYN547407: An Evaluation of A21550B for control of Lepidoptera in Turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246872 2019, ISM-555: Greenhouse evaluation of foliar applications - Tetranychus mites, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246873 2019, ISM-555: Nursery and greenhouse crop safety evaluation (lantana), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246874 2019, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246875 2019, ISM-555: Greenhouse evaluation of foliar applications to non-blooming plants - thrips, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246876 2019, ISM-555: Greenhouse evaluation of foliar applications to non-blooming plants - thrips, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246877 2020, ISM-555: Greenhouse evaluation of foliar applications to non-blooming plants - thrips (Chili thrips on gerbera), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246878 2019, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding pests (lantana lace bug), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246879 2019, ISM-555: Greenhouse evaluation of curative foliar applications - leaf miner larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246880 2020, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding lepidoptera, etc.(Bougainvillea looper), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246881 2020, ISM-555: Greenhouse evaluation of foliar applications - non-Tetranychus mites (Broad on NG Impatiens), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246882 2020, ISM-555: Nursery and greenhouse crop safety evaluation (woodies), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246883 2019, ISM-555: Nursery and greenhouse crop safety evaluation (Woodies), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246884 2019, ISM-555: Nursery and greenhouse crop safety evaluation (annuals), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246885 2020, ISM-555: Nursery and greenhouse crop safety evaluation (non-woody), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246886 2019, ISM-555: Greenhouse evaluation of foliar applications - non-Tetranychus mites (broad mites), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246887 2020, ISM-555: Greenhouse evaluation of cold fog applications (thrips), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246888 2019, ISM-555: Greenhouse evaluation of foliar applications to non-blooming plants - thrips, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246889 2019, ISM-555: Greenhouse evaluation of foliar applications - Tetranychus mites, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246890 2021, ISM-555: Greenhouse evaluation of foliar applications - Tetranychus mites, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246891 2018, ISM-555: Evaluate A21708C and A21377W for control of billbugs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246892 2021, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding pests. Adult Black Vine Weevil Dropped 1DAT, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246893 2016, SYN547407: An Evaluation of A21550B for control of Billbug Larvae in Turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246894 2021, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding pests, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246895 2019, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246896 2021, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246897 2016, SYN547407: An Evaluation of A21550B for control of Lepidoptera in Turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246898 2016, SYN547407: An Evaluation of A21550B for control of Billbug Larvae in Turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246899 2018, ISM-555: Evaluate A21708C and A21377W for control of billbugs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246900 2017, ISM-555: Evaluate A21708C and A21377W for control of Lepidoptera in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246901	2019, Evaluation of A22431A for residual control of Lepidopteran pests in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246902	2018, ISM-555: Evaluation of A21377X for control of Lepidoptera in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246903	2021, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246904	2020, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246905	2017, ISM-555: Evaluate A21708C and A21377W for control of Lepidoptera in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246906	2019, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246910	2017, ISM-555: Evaluation of A21708C and A21377W for control of annual bluegrass weevil in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246911	2018, ISM-555: Evaluate A21377X for control of emerging overwintering ABW adults, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246912	2016, A21550B: Evaluation for control of annual bluegrass weevil adults in turfgrass, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246913	2017, ISM-555: Evaluation of A21708C and A21377W for control of annual bluegrass weevil in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246914	2018, ISM-555: Evaluate A21377X for control of emerging overwintering ABW adults, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246915	2016, A21550B: Evaluation for control of annual bluegrass weevil adults in turfgrass, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246916	2017, ISM-555: Evaluation of A21708C and A21377W for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246917	2018, ISM-555: Evaluation of A21377X for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246918	2017, ISM-555: Evaluation of A21708C and A21377W for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246919	2018, ISM-555: Evaluation of A21377X for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246920	2017, ISM-555: Evaluation of A21708C and A21377W for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246921	2018, ISM-555: Evaluation of A21377X for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3246922	2018, ISM-555: Evaluation of A21377X for control of annual bluegrass weevil larvae in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246923 2018, ISM-555: Evaluate A21377X for control of emerging overwintering ABW adults, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246924 2017, ISM-555: Evaluation of formulations for control of annual white grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246925 2017, ISM-555: Evaluation of formulations for control of annual white grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246927 2020, Evaluate ISM-555 for control of annual bluegrass weevil larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246928 2020, Evaluation of ISM-555 for control of late instar ABW larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246929 2020, Evaluate ISM-555 for control of annual bluegrass weevil larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246930 2020, Evaluate ISM-555 for control of annual bluegrass weevil larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246931 2020, Evaluation of ISM-555 for control of late instar ABW larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246932 2020, Evaluation of ISM-555 and diamide formulations for white grub control - preventative timing, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246933 2019, Evaluate ISM-555 for control of annual bluegrass weevil adults, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246934 2019, Evaluate ISM-555 for control of annual bluegrass weevil adults, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246935 2019, Evaluate ISM-555 for control of annual bluegrass weevil larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246936 2019, Evaluate ISM-555 for control of annual bluegrass weevil larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246937 2019, Evaluate ISM-555 for control of annual bluegrass weevil larvae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246938 2019, ISM-555: Nursery and greenhouse crop safety evaluation, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246939 2019, Evaluation of A22431A for preventative control of white grubs in turf, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3246940 2019, ISM-555: Nursery and greenhouse evaluation of foliar applications - leaf feeding pests, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3459237 2023, A23294 TO (Sub. No. 2021-3049) Deficiency Response, DACO: 10.1

3459238 2020, ISM-555: Greenhouse evaluation of foliar applications - non-Tetranychus mites, DACO: 10.2.3.3

3459239 2020, ISM-555: Greenhouse evaluation of foliar applications - non-Tetranychus mites, DACO: 10.2.3.3

3459240 2021, ISM-555: Greenhouse evaluation of foliar applications to non-blooming plants - thrips, DACO: 10.2.3.3