Proposed Registration Decision PRD2026-09

Spiropidion, A20262 Insecticide

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Overview

Proposed registration decision for spiropidion

Health Canada, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Spiropidion Technical Insecticide, and A20262 Insecticide, containing the active ingredient spiropidion, to control or suppress aphids, whiteflies, mealybugs, and two-spotted spider mites on terrestrial food and feed crops, and greenhouse food crops.

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 spiropidion and A20262 Insecticide.

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 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 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 the Health Canada 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 spiropidion and A20262 Insecticide, Health Canada 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 spiropidion and A20262 Insecticide, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

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

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

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*.

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

What is spiropidion?

Spiropidion is a new tetramic acid insecticide that inhibits lipid biosynthesis and is mainly active through ingestion, showing very little activity through contact. This active ingredient has translaminar and systemic activity in plants, moving to both untreated new growth and the roots. Spiropidion affects egg production in females and immature stages of insects and is used against various sucking insect pests on a wide array of crops.

Health considerations

Can approved uses of spiropidion affect human health?

A20262 Insecticide, containing spiropidion, is unlikely to affect your health when used according to proposed label directions.

Potential exposure to spiropidion may occur through the diet (food and drinking water), when handling and applying the end-use product, and 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 parents). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose 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 spiropidion was of low acute toxicity by the oral and dermal routes of exposure, and was non-irritating to the eyes and skin. It was of slight acute toxicity via the inhalation route of exposure and caused an allergic skin reaction. Consequently, the signal word “CAUTION” and the hazard statements “POISON” and “POTENTIAL SKIN SENSITIZER” are required on the label.

The acute toxicity of the end-use product A20262 Insecticide, containing spiropidion, was low via the oral, dermal and inhalation routes of exposure. It 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.

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 spiropidion to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on body weight, cholesterol and fetal development. 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.

Residues 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 indicated that the general population are exposed to less than 20% of the acute reference dose for spiropidion, and therefore are not of health concern. Aggregate acute dietary (food plus drinking water) intake estimates indicated that females 13–49 are exposed to less than 78% of the acute reference dose for spiropidion, and therefore are not of health concern.

Aggregate chronic dietary (food plus drinking water) intake estimates indicated that the general population and all population subgroups are exposed to less than 21% of the acceptable daily intake for spiropidion, and therefore are not of health concern.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Given that dietary risks from the consumption of foods are shown to be acceptable when spiropidion is used according to the supported label directions, MRLs are being proposed as a result of this assessment (refer to PMRL2025-07, *Spiropidion*).

MRLs for spiropidion were determined from the acceptable residue trials conducted throughout Canada and/or the United States on potatoes, leaf lettuce, head lettuce, spinach, mustard greens, broccoli, cabbage, cauliflower, Brussels sprouts, greenhouse-grown tomatoes, peppers and cucumbers, orange, lemon, grapefruit, apple, pear, grape, and cottonseed can be found in the Science evaluation of this document.

Occupational risks from handling A20262 Insecticide

Occupational risks are not of health concern when A20262 Insecticide is used according to the proposed label directions, which include protective measures.

Workers mixing, loading or applying A20262 Insecticide, and workers entering recently treated fields, orchards, vineyards and greenhouses can be exposed to spiropidion residues through direct skin contact or through inhalation. Therefore, the label specifies that anyone mixing, loading and applying A20262 Insecticide must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. The label also requires that workers do not enter or be allowed into treated areas during the restricted-entry interval (REI) of 12 hours except for certain activities conducted in treated leafy and brassica head and stem vegetables and grapes, which require extended REIs. 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 A20262 Insecticide are not of health concern when the end-use product is used according to the proposed label directions, including extended REIs.

Health risks in residential and other non-occupational environments

Risks in residential and other non-occupational environments are not of health concern when A20262 Insecticide is used according to the proposed label directions.

Adults and children can come into direct contact with spiropidion residues when pome fruit trees on pick-your-own farms or residential properties are treated with A20262 Insecticide. 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 product is used according to the label directions.

Health risks to bystanders

Bystander risks are not of health concern when A20262 Insecticide is used according to the proposed label directions and spray drift restrictions are observed.

A standard label statement to protect against drift during application is on the label. Therefore, health risks to bystanders are not of concern when the end-use product is used according to the proposed label directions.

Environmental considerations

What happens when spiropidion is introduced into the environment?

When used according to label directions, environmental risks associated with spiropidion and its associated end-use product are acceptable.

Spiropidion enters the environment when its end-use product, A20262 Insecticide, is used to control aphids, whiteflies, mealybugs and two-spotted spider mites in labelled crops. Spiropidion is quickly broken down by water and microorganisms to form the transformation product, SYN547305. SYN547305 is further converted into several other transformation products, which are less toxic to the environment than spiropidion and SYN547305.

Spiropidion and its transformation products may move through soil to reach groundwater. They may also move off the treatment area in runoff to reach surface water. Spiropidion and its transformation products are not expected to be released into the air in significant quantities or to accumulate in the tissue of animals.

Without risk mitigation measures, the use of spiropidion at the proposed rates may cause adverse effects to aquatic organisms, bees and non-target terrestrial plants. The required risk mitigation measures to reduce risks to these organisms are described below. After a scientific review of the available information, Health Canada has concluded that environmental risks from the proposed uses of spiropidion are acceptable when used according to the label directions, which include the required risk mitigation measures.

Value considerations

What is the value of A20262 Insecticide?

A20262 Insecticide provides a new active ingredient for control of listed sucking pests on a wide variety of crops. A20262 Insecticide may contribute to the resistance management of pests by providing a new alternative that can be used in rotation with existing products.

A20262 Insecticide provides control or suppression of aphids, whitefly, two-spotted spider mites, and/or mealybugs on various leafy, brassica, stem, fruiting, and cucurbit vegetables both in the field and in greenhouses, as well as on grapes and pome fruits. While another Group 23 insecticide, spirotetramat, is registered for the pest/crop combinations listed on the A20262 Insecticide label, Group 23 insecticides are not known to have cross-resistance with other insecticide groups.

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 label of Spiropidion Technical Insecticide and A20262 Insecticide to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

To reduce the potential exposure of workers to spiropidion through direct skin contact, workers mixing, loading and applying A20262 Insecticide and performing cleaning and repair activities must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. Risks to workers and those exposed in residential and non-occupational environments are not of health concern when A20262 Insecticide is used according to the proposed label directions and restricted-entry intervals (REIs) are observed. Furthermore, a standard label statement to protect against drift during application is present on the label.

Environment

- Precautionary label statements indicating toxicity to aquatic organisms, bees and non-target terrestrial plants.
- Application of spiropidion to highly bee attractive field crops (pome fruit) is not permitted during bloom.
- Application to fruiting vegetables and cucurbit vegetables is restricted to the evening when most bees are not foraging.
- Label statements advising users that spiropidion may harm brood of bees used in greenhouse production and that application should be avoided when bees are in the treatment area.

- Spray buffer zones up to 2 metres to protect sensitive aquatic and terrestrial habitat.
- Precautionary label statements with instructions to reduce runoff and leaching to groundwater.

Next steps

Before making a final registration decision on spiropidion and A20262 Insecticide, Health Canada 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 5 July 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 Pesticides 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 Pesticides Publications Section, 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

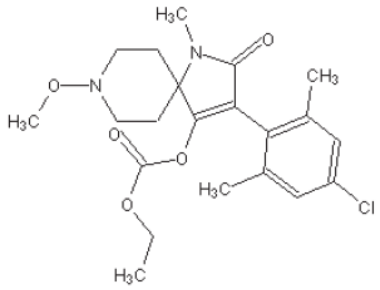
When Health Canada makes its registration decision, it will publish a Registration Decision on spiropidion and A20262 Insecticide (based on the Science evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the Pesticides Regulatory Directorate's Reading Room. For more information or if you have questions, please contact the Pesticides Information Service.

Science evaluation

Spiropidion, A20262 insecticide

1.0 The active ingredient, Its properties and uses

1.1 Identity of the active ingredient

Active substance	Spiropidion
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	3-(4-chloro-2,6-dimethylphenyl)-8-methoxy-1-methyl-2-oxo-1,8-diazaspiro[4.5]dec-3-en-4-yl ethyl carbonate
2. Chemical Abstracts Service (CAS)	3-(4-chloro-2,6-dimethylphenyl)-8-methoxy-1-methyl-2-oxo-1,8-diazaspiro[4.5]dec-3-en-4-yl ethyl carbonate
CAS number	1229023-00-0
Molecular formula	$C_{21}H_{27}ClN_2O_5$
Molecular weight	422.9
Structural formula	
Purity of the active ingredient	98.3%

1.2 Physical and chemical properties of the active ingredients and end-use product

Technical product—Spiropidion technical insecticide

Property	Result
Colour and physical state	Off-white powder
Odour	Odourless
Melting range	134.20–134.31°C
Boiling point or range	Not applicable to a solid.
Density	1.29 g/cm^3 at 20°C
Vapour pressure at 20°C	< 0.005 mPa

Property	Result			
Ultraviolet (UV)-visible spectrum	Solution	Wavelength (nm)	Absorbance	Molar extinction coefficient [1/mol*cm]
	Neutral	225 290	0.5297 0.0303	17 048 975
	Acidic	225 290	0.5089 0.0057	16 379 183
	Basic	273 290	0.3758 0.2557	12 095 8229
	No significant absorption at or above 300 nm			
Solubility in water at 20°C	0.046 g/L			
Solubility in organic solvents at 20°C	Solvent: Solubility (g/L) Acetone: 360 Dichloromethane: > 500 Ethyl acetate: 300 Hexane: 3.4 Methanol: 250 Octanol: 50 Toluene: 320			
n-Octanol-water partition coefficient (K_{ow})	log K_{ow} = 3.3			
Dissociation constant (pK_a)	The active ingredient will be unionized at environmental pH range of 4 to 10.			
Stability (temperature, metal)	Stable when stored in a steel drum with inner varnish, polyethylene bags, high-density polyethylene (HDPE) packs, paper/polyethylene terephthalate/aluminum/polyethylene bags for 2 weeks at 54°C and for a year at 20°C. The active ingredient is stable for 2 weeks at 54°C when stored in glass. Stable to metals (aluminum and iron) and metal ions (aluminum acetate and iron (II) acetate) for 7 and 14 days at 20°C ± 2°C and at 40°C ± 2°C. Stable to tin, galvanized metals, steel and stainless steel for 7 days at 54°C ± 2°C.			

End-use product—A20262 insecticide

Property	Result
Colour	Off-white
Odour	Characteristic odour
Physical state	Liquid
Formulation type	Suspension
Label concentration	Spiropidion at 300 g/L

Property	Result
Container material and description	HDPE and fluorinated HDPE jugs or drums: 1 to 100 L
Density	1.09 g/mL at 20˚C
pH of 1% dispersion in water	5.3 (1% in water)
Oxidizing or reducing action	The product is compatible with oxidizing and reducing agents.
Storage stability	The active ingredient is stable in HDPE and fluorinated HDPE for 14 days at 54˚C
Corrosion characteristics	Not corrosive to its HDPE and fluorinated HDPE packaging.
Explodability	Not explosive

1.2 Directions for use

A20262 Insecticide is applied to crop group (CG) 4-13 (Leafy Vegetables (excluding watercress)), CG 5-13 (*Brassica* Head and Stem Vegetables), CG 8-09 (Fruiting Vegetables) and CG 9 (Cucurbit Vegetables) for the control of aphids and whiteflies at 0.3 to 0.6 L product per ha (90 to 180 g a.i. per ha), in a minimum of 200 L water per ha. Applications for suppression of aphids in CG 11-09 (Pome Fruits) are made at a rate of 0.33 to 0.67 L product per ha (100 to 200 g a.i. per ha), applied by foliar airblast in a water volume of 400 to 4000 L product per ha. A20262 Insecticide is applied for control of mealybugs in grape at a rate of 0.5 to 0.7 L product per ha (150 to 200 g a.i. per ha) by foliar airblast in 500 to 1000 L spray per ha. Applications for control of aphids, whiteflies, and two-spotted spider mite in greenhouse tomatoes, peppers, eggplant, and cucumbers is accomplished at a rate of 0.3 to 0.48 L product per ha (90 to 144 g a.i. per ha) by foliar sprayer or hand boom in a water volume of 300 to 2000 L per ha. A20262 Insecticide is applied with a methylated seed oil (MSO) adjuvant. All outdoor uses may be applied with up to 2 consecutive foliar sprays and a maximum of 3 applications per year, applied at least 7 days apart. Greenhouse applications are limited to a maximum of 2 applications per year.

1.3 Mode of action

A20262 Insecticide is a suspension formulation insecticide that contains the active ingredient spiropidion (300 g/L). Spiropidion is a novel insecticide belonging to the tetramic acid chemical class. This active ingredient inhibits lipid biosynthesis by acting on the enzyme acetyl-CoA carboxylase (ACCase) and is categorized under the IRAC Group 23 (inhibitors of acetyl-CoA carboxylase) mode of action. This active ingredient is mainly active through ingestion and shows very little activity through contact. Spiropidion demonstrates translaminar control of insects and is two-way systemic in the plant (phloem and xylem mobile). Inside the plant, it moves to both the untreated new growth and, to a lesser extent, the roots. Spiropidion is efficacious on immature stages of insect development and on egg production of females, and has activity against a variety of sucking pests.

2.0 Methods of analysis

2.1 Methods for analysis of the active ingredient

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

2.2 Method for formulation analysis

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

2.3 Methods for residue analysis

High performance liquid chromatography methods with tandem mass spectrometric detection (HPLC-MS/MS; enforcement method QuEChERS/BPL19-0035; data gathering methods GRM069.02A, GRM069.04A, GRM069.08A, GRM069.10A, GRM069.11A, GRM069.12A, and GRM069.18A) were developed and proposed for data generation and enforcement purposes in primary crops, rotational crops, and processed commodities. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in all tested plant matrices. Adequate extraction efficiencies were demonstrated using radiolabelled samples (primary crops: cotton, potato, and tomato) analyzed with the enforcement method. Methods for residue analysis in plant matrices are summarized in Appendix I, Table 1.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

Spiropidion technical insecticide, also known as SYN546330, is a pro-insecticide belonging to the tetramic acid chemical class. As a pro-insecticide, the enol ethyl carbonate group on spiropidion is cleaved in the target pest to release the active principal (SYN547305) which binds to the target site in insects. The insecticidal mode of action (MOA) of spiropidion involves inhibition of the acetyl CoA carboxylase enzyme, leading to the suppression of lipid biosynthesis.

A detailed review of the toxicology database for spiropidion was conducted. The majority of the toxicology database for spiropidion was reviewed and summarized previously in the Evaluation Report for submission 2020-4760. New information considered for the current applications included acute toxicity studies conducted with the end-use product A20262 Insecticide, as well as non-oral acute toxicity studies (including acute dermal and inhalation, eye and skin irritation, and dermal sensitization) and a 28-day dermal toxicity study in rats conducted with spiropidion. A rationale to waive the conditional requirement for a repeat-exposure inhalation toxicity study for spiropidion was also provided, along with additional studies to support this waiver request that included a toxicokinetics study conducted in rats via the inhalation route, an airway irritation study using an in vitro model of human airway epithelium derived from human airway cells, and

a 5-day inhalation tolerability study in rats. Limited genotoxicity studies were also provided for the plant metabolite SYN549098. Additionally, the applicant submitted rationales for revising certain previous Health Canada conclusions pertaining to the results of various toxicity studies. Overall, the scientific quality of the data is acceptable and the database is considered adequate to characterize the potential health hazards associated with Spiropidion Technical Insecticide. A search of the published literature did not identify any information relevant to the hazard characterization of spiropidion.[5]

The previous assessment of the toxicology database for spiropidion revealed that the principal effects following repeated oral dosing were decreases in body weight and body weight gain, thyroid gland toxicity, including findings of increased weight, follicular cell hypertrophy, and colloid contractions, and changes in certain clinical chemistry parameters consistent with the insecticidal MOA of spiropidion, such as decreased cholesterol, protein, and triglycerides. The overall weight of evidence suggested that spiropidion was not genotoxic or carcinogenic. There were no treatment-related effects observed in the offspring or on reproductive endpoints assessed in the available 2-generation reproductive toxicity study. In developmental toxicity studies, sensitivity of the young was noted in both rats and rabbits as variations of the skeletal system were observed in fetuses at dose levels that did not result in any adverse effects on maternal animals. More details on the results of the previously assessed toxicology studies can be found in the Evaluation Report for submission 2020-4760.

In addition to being of low acute oral toxicity, the technical grade active ingredient, spiropidion, was of low and slight acute toxicity in rats via the dermal and inhalation routes of exposure, respectively. Spiropidion was non-irritating to the eyes and skin of rabbits, but was positive for dermal sensitization in mice when tested using the LLNA.

In acute toxicity studies, the end-use product A20262 Insecticide was of low acute toxicity via the oral, dermal, and inhalation routes of exposure in rats. A20262 Insecticide was non-irritating: to the eyes and skin of rabbits, when tested in vivo; and, when using isolated chicken eyes and reconstructed human epidermis, when tested in vitro. When tested for dermal sensitization using the local lymph node assay (LLNA) in mice, A20262 Insecticide yielded a positive result.

The effects observed in the 28-day dermal toxicity study in rats were consistent with those seen in repeat-dose oral toxicity studies conducted with spiropidion, and included decreased cholesterol at all dose levels, along with reduced body weight gain and increased thyroid gland hypertrophy at higher doses.

In the acute inhalation toxicokinetics study, in which rats were exposed nose-only to non-radiolabelled spiropidion, levels of spiropidion in plasma were not quantifiable whereas the maximum level of the enol metabolite occurred at or before the end of the 6-hour exposure. In the in vitro airway irritation study, spiropidion induced evidence of irritation at the highest concentrations tested as evidenced by thinning of the membrane and necrosis of respiratory epithelium, but no toxicity to the epithelium was evident based on the parameters examined. In the 5-day inhalation tolerability study, reduced body weight occurred at the lowest exposure concentration tested, while higher concentrations elicited significant toxicity in the form of mortality.

[5] Search conducted December 29, 2025 using PubMed and the keyword “spiropidion”.

The request to waive the conditional requirement for a repeat-exposure inhalation toxicity study was granted based on weight of evidence considerations that suggested that such a study is unlikely to provide information critical to assessing potential risks from inhalation exposure to spiropidion. This was based on the fact that the critical endpoints of concern observed in the spiropidion database were effects on the developing fetus, for which the point of departure was determined to be comparable to the internal dose level that would result from exposure to the lowest concentration recommended for the conduct of a subchronic inhalation toxicity study in rats.

Genotoxicity studies with SYN549098 (2-(4-chloro-2,6-dimethyl-phenyl)-2-hydroxy-N-methyl-acetamide), a metabolite found primarily in rotational crops, were negative in all available studies including in vitro studies for reverse mutations in bacteria, forward mutations in mammalian cells, and induction of micronuclei in human lymphocytes.

The applicant provided scientific rationales to support revisiting Health Canada's conclusions related to various toxicity studies assessed during the previous evaluation of spiropidion. As a result of this re-assessment, the no-observed-adverse-effect-level (NOAEL) established in the 1-year oral toxicity study in dogs was revised. Previously, a decrease in the mean body weight of females was noted at 10 mg/kg bw/day. Upon further consideration, the body weights of females at this dose were within the variability of data for the control group throughout the duration of the study. Therefore, this apparent decrease in body weight is considered to be the result of normal biological variation. As no other adverse effects were present at this dose level, the NOAEL in females has been revised to 10 mg/kg bw/day. Furthermore, since this endpoint was the basis of the previously established acceptable daily intake (ADI), the endpoint selection for this reference value has also been updated, as discussed in section 3.2.4 below.

In the Evaluation Report for submission 2020-4760, there was a minor error in the way in which maternal effects were reported in the rabbit developmental toxicity study. Previously, it was indicated that effects at the maternal lowest-observed-adverse-effect level (LOAEL) included decreased body weight gain and slight decreases in food consumption, and that the effect at 60 mg/kg bw/day was body weight loss. However, the dose of 60 mg/kg bw/day and the body weight loss was the basis for the maternal LOAEL, and the decreased body weight gain and slight reduction in food consumption were deemed non-adverse and occurred at the dose level of 30 mg/kg bw/day. The reporting of maternal effects in this study have been corrected in Appendix I, Table 3.

The toxicology reference values for use in the human health risk assessment are summarized in Appendix I, Table 2. Results of studies conducted on laboratory animals with spiropidion that were new to the current assessment, or revised from the previous assessment under submission 2020-4760, are summarized in Appendix I, Table 3. The results of the acute toxicity studies conducted with the end-use product A20262 Insecticide are summarized in Appendix I, Table 4.

3.1.2 *Pest Control Products Act* hazard characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of,

and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.[6]

The characterization of the PCPA factor for spiropidion was outlined previously in the Evaluation Report for submission 2020-4760. With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contains the full complement of required studies including gavage developmental toxicity studies in the rabbit and rat, and a dietary reproductive toxicity study in the rat.

In the rat developmental toxicity study, higher incidences of bifurcation of the sternum xiphoid cartilage, ossified phalanges, and incomplete ossification of the fifth sternebra were observed in rat fetuses in the absence of maternal toxicity. Similarly, in the rabbit developmental toxicity study, increased incidences of incomplete cartilaginous dorsal plate of the second cervical vertebra and incomplete sternum xiphoid cartilage were observed in the absence of maternal toxicity.

Overall, the database is adequate for determining the sensitivity of the young. Sensitivity of the young was evident in the rat and rabbit developmental toxicity studies with increased incidences of skeletal variations occurring in the absence of maternal toxicity. These effects were not considered serious in nature. On this basis, the PCPA factor was reduced to threefold for scenarios in which the variations from the rat or rabbit developmental toxicity studies are used to establish the point of departure for risk assessment. For other exposure scenarios, the PCPA factor was reduced to onefold.

3.2 Toxicology reference values

3.2.1 Route and duration of exposure

For mixers, loaders and applicators, occupational exposure to A20262 Insecticide is characterized as short-term (< 30 days) to long-term (up to 1 year) in duration and is predominantly by the dermal and inhalation routes. For postapplication workers, occupational exposure to A20262 Insecticide is characterized as short- to intermediate-term (30 days to < 6 months) in duration for field uses and long-term for greenhouse uses. The route of exposure is predominantly by the dermal route due to the low vapour pressure of spiropidion. For residential exposure scenarios, contact with pome fruit trees treated with A20262 Insecticide would occur primarily via the dermal route of exposure and for a short-term duration only.

3.2.2 Occupational and residential toxicology reference values

Short- to long-term dermal and inhalation - Adults > 16 years old

For short-, intermediate- and long-term residential and occupational exposures of adults via the dermal and inhalation routes, the developmental NOAEL of 10 mg/kg bw/day from the rat and rabbit oral developmental toxicity studies was selected. At the developmental LOAEL of 30 mg/kg bw/day in the rat study, higher incidences of ossified phalanges, bifurcated sternum xiphoid cartilage and incomplete ossification of the fifth sternebra were observed. At the

[6] SPN2008-01, The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides.

developmental LOAEL of 30 mg/kg bw/day in the rabbit study, higher incidences of incomplete cartilaginous dorsal plate of the second cervical vertebra and incomplete sternum xiphoid cartilage were observed. These developmental findings occurred in the absence of maternal toxicity. Worker populations could include pregnant people and therefore these endpoints were considered appropriate for the occupational risk assessment. A repeat-exposure inhalation toxicity study was not available and the available 28-day dermal toxicity study did not assess the relevant endpoints of concern (that is, developmental effects following prenatal exposure), thus necessitating the use of an oral toxicity study for risk assessment purposes.

For residential scenarios, the target margin of exposure (MOE) for this endpoint is 300. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to threefold. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed parents.

For occupational scenarios, the target MOE for this endpoint is 300. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. Worker populations could include pregnant or lactating people and therefore these endpoints were considered appropriate for the occupational risk assessment. In light of concerns regarding prenatal toxicity, as outlined in the *Pest Control Products Act* hazard characterization section, an additional threefold factor was applied to this endpoint to protect for a sensitive subpopulation, namely people who may become pregnant.

Short-term dermal – Children 6 to 11 years old

For short-term residential dermal exposure of children 6 to 11 years old, the LOAEL of 100 mg/kg bw/day for male rats in the 28-day dermal toxicity study was selected. At this dose level, a mild decrease in cholesterol was observed. This study was conducted via the relevant route and was of an appropriate duration of exposure. The developmental variations selected for assessing risks to adults are not relevant to this age group, whereas the observed endpoint in the 28-day dermal toxicity study was deemed appropriate for assessing risks to children. The target MOE for this scenario is 100. Tenfold factors were applied each for interspecies extrapolation and intraspecies variability. As outlined in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to onefold. An additional uncertainty factor for lack of a NOAEL was not applied as the nature and severity of the effect at the LOAEL suggested the LOAEL was occurring near the threshold of toxicity.

3.2.3 Acute reference dose (ARfD)

Females 13 to 49 years old

The rat developmental toxicity study and the rabbit developmental toxicity study were selected as co-critical studies to estimate the acute dietary risk for females 13 to 49 years old. The developmental NOAEL of 10 mg/kg bw/day from the rat and rabbit developmental toxicity studies was selected. At the developmental LOAEL of 30 mg/kg bw/day in the rat study, higher incidences of ossified phalanges, bifurcated sternum xiphoid cartilage and incomplete ossification of the fifth sternebra were observed. At the developmental LOAEL of 30 mg/kg bw/day in the rabbit study, higher incidences of incomplete cartilaginous dorsal plate of the

second cervical vertebra and incomplete sternum xiphoid cartilage were observed. These developmental findings occurred in the absence of maternal toxicity. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to threefold. The composite assessment factor (CAF) is thus 300. The ARfD is calculated according to the following formula:

$$\text{ARfD (females 13 to 49 years old)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{10 \text{ mg/kg bw/day}}{300} = 0.03 \text{ mg/kg bw of spiropidion}$$

General population (excluding females 13 to 49 years old)

To estimate the acute dietary risk for the general population, the maternal NOAEL of 30 mg/kg bw/day from the rat and rabbit developmental toxicity studies was selected. At the maternal LOAEL of 60 mg/kg bw/day, body weight loss was observed within the first few days of dosing in both studies. The selection of this point of departure is also supported by the effects in the supplemental 28-day oral toxicity study in the dog, in which no adverse effects were observed at the mid-dose level of 30 mg/kg bw/day, whereas animals administered the high dose of 100 mg/kg bw/day were euthanized after one or two doses due to adverse clinical signs. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to onefold. The CAF is thus 100. The ARfD is calculated according to the following formula:

$$\text{ARfD (general population)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{30 \text{ mg/kg bw/day}}{100} = 0.3 \text{ mg/kg bw of spiropidion}$$

3.2.4 Acceptable daily intake (ADI)

Previously, the ADI was established at 0.03 mg/kg bw/day, based on the NOAEL of 3 mg/kg bw/day from the 1-year oral toxicity study in dogs, and a CAF of 100, comprised of the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability and a PCPA factor of onefold. As the NOAEL in the 1-year dog study has been revised to 10 mg/kg bw/day, reconsideration of the previous ADI was undertaken for the current assessment. When factoring in the appropriate assessment factors, including the PCPA factor, the developmental NOAEL of 10 mg/kg bw/day from the rat and rabbit developmental toxicity studies provides the greatest protection against the effects noted in the database, and was therefore selected for the current assessment to estimate risk following repeated dietary exposure. At the developmental LOAEL of 30 mg/kg bw/day in the rat study, higher incidences of ossified phalanges, bifurcated sternum xiphoid cartilage and incomplete ossification of the fifth sternebra were observed. At the developmental LOAEL of 30 mg/kg bw/day in the rabbit study, higher incidences of incomplete cartilaginous dorsal plate of the second cervical vertebra and incomplete sternum xiphoid cartilage were observed. These developmental findings occurred in the absence of maternal toxicity. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* hazard characterization section, the PCPA factor was reduced to threefold. The CAF is thus 300. The revised ADI is calculated according to the following formula:

$$ADI = \frac{NOAEL}{CAF} = \frac{10\ mg/kg\ bw/day}{300} = 0.03\ mg/kg\ bw/day\ of\ spiropidion$$

3.2.5 Cancer assessment

There was no evidence of tumourigenicity and therefore, a cancer risk assessment was not necessary.

3.2.6 Aggregate toxicology reference values

Aggregate exposure is the total exposure to a single pesticide that may occur from dietary (food and drinking water), residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation). Short-term aggregate exposure to spiropidion may be comprised of food and residential exposure via the dermal route.

The toxicology endpoint selected for aggregation for adults (>16 years old) was skeletal variations in the absence of maternal toxicity. For the oral and dermal routes, the developmental NOAELs of 10 mg/kg bw/day from the rat and rabbit oral developmental toxicity studies were selected with a target MOE of 300. The PCPA factor for all routes was threefold as set out in the *Pest Control Products Act* hazard characterization section.

The toxicology endpoint selected for aggregation for children (6 to 11 years old) was decreased cholesterol. For the oral route, the NOAEL of 6.2 mg/kg bw/day from the oral 90-day rat toxicity study was selected with a target MOE of 100. For the dermal route, the LOAEL of 100 mg/kg bw/day from the 28-day dermal rat toxicity study was selected with a target MOE of 100. The PCPA factor for all routes was onefold as set out in the *Pest Control Products Act* hazard characterization section.

3.3 Dermal absorption

A triple pack, consisting of a rat in vivo study (PMRA No. 3395885), and a rat and human in vitro study (PMRA No. 3395886) was submitted. These studies were reviewed and considered acceptable for the selection of a dermal absorption value for the exposure and risk assessment. The triple pack showed that the in vitro model was predictive of absorption in vivo, which supports the current Health Canada position of accepting in vitro studies alone, when conducted using the standard methodology. For spiropidion, the selection of a dermal absorption value from the human in vitro study (Appendix I, Table 5) was considered acceptable based on an analysis of the factors that can impact absorption (such as formulation, product composition, doses). As such, a dermal absorption value of 11% was selected from the lowest spray dilution dose in the human in vitro study for all exposure scenarios.

3.4 Occupational and residential exposure assessment

3.4.1 Acute hazards of end-use product and mitigation measures

3.4.1.1 A20262 Insecticide

The acute hazard assessment indicated that A20262 Insecticide is considered to have low acute oral, dermal and inhalation toxicity. It is non-irritating to eyes and skin and is a potential dermal

sensitizer. Based on these acute hazards, a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves are required for workers during mixing, loading, application, clean-up, and repair.

3.4.2 Occupational exposure and risk assessment

3.4.2.1 Mixer, loader and applicator exposure and risk assessment

Individuals have potential for exposure to spiropidion during mixing, loading, application, clean-up, and repair. 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 A20262 Insecticide to various crops using groundboom, airblast, and handheld sprayers. The PPE in the risk assessment is based on handlers wearing a long-sleeved shirt, long pants, socks, shoes, and chemical-resistant gloves (Appendix I, Table 6).

Dermal exposure was estimated by combining the unit exposure values with the amount of product handled per day and the dermal absorption value of 11%. Inhalation exposure was estimated by combining the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight.

Exposure estimates were compared to the selected toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 300. Dermal and inhalation MOEs were combined, since the dermal and inhalation reference values are based on the same toxicological effects. Calculated MOEs are greater than the target MOE of 300 for all chemical handler scenarios and are therefore not of health concern (Appendix I, Table 7).

3.4.2.2 Postapplication exposure and risk assessment

There is potential for exposure to workers entering areas treated with A20262 Insecticide to complete tasks such as hand harvesting, hand weeding, girdling/turning etc. Given the nature of activities performed, exposure should be primarily via the dermal route based on dermal contact with treated foliage. Inhalation exposure is not expected as spiropidion is considered non-volatile with a vapour pressure of $< 5 \times 10^{-9}$ kPa at 25ºC, which is less than the North American Free Trade Agreement (NAFTA) criterion for a non-volatile product for outdoor scenarios (1×10^{-4} kPa at 20–30°C) and indoor scenarios (1×10^{-5} kPa at 20–30°C). As such, a quantitative inhalation risk assessment is not required. Inhalation risk is not of health concern for postapplication workers as spiropidion is considered to be non-volatile and the restricted-entry intervals will allow residues to dry, suspended particles to settle, and vapours to dissipate.

Dermal exposure to workers entering treated areas is estimated by combining 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). As chemical-specific DFR data were not submitted, a standard DFR value of 25% of the application rate coupled with 10% daily dissipation of residues were used in the exposure assessment, except for greenhouse uses, which used a 2% daily dissipation rate of residues.

Exposure estimates were compared to the toxicological reference value to obtain the margin of exposure (MOE); the target MOE is 300. REIs of 16 days for girdling/turning and 8 days for hand harvesting/hand leaving pulling/tying/training in grapes are required to meet the target MOE of 300. A 3-day REI for hand harvesting of brassica head and stem vegetables and a 1-day REI for hand weeding in leafy and brassica head and stem vegetables are also required to meet the target MOE of 300. For all other postapplication activities, covered by those listed in Appendix I, Table 8, the REI of 12 hours is adequate.

3.4.3 Residential exposure and risk assessment

3.4.3.1 Handler exposure and risk assessment

A20262 Insecticide is not a domestic class product and is not permitted for use in residential settings; therefore, a residential handler exposure assessment is not required.

3.4.3.2 Postapplication exposure and risk assessment

A20262 Insecticide is proposed for use on pick-your-own (PYO) and pome fruit trees which includes residential areas. As such, a postapplication residential risk assessment is required.

3.4.3.2.1 Pick-Your-Own (PYO) activities

Given that pome fruits can be treated with spiropidion, 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 A20262 Insecticide

When a commercial applicator is hired to treat pome fruit trees in a residential area or a farmer treats pome fruit 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 old and over) and children (6 to less than 11 years old) when contacting treated fruit trees to perform activities such as hand harvesting, thinning, pruning, etc.

Dermal exposure was estimated using the standard DFR values, 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 and toxicological reference values, calculated MOEs were greater than the target MOEs of 300 for adults and 100 for children (Appendix 1, Table 9) for all residential postapplication exposure scenarios on Day 0. As such, health risks are not of concern and the individuals can enter the treated area once 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 origin

In primary crops, the residue definition for enforcement is spiropidion and its metabolite SYN547305 (expressed as parent equivalents). The residue definition for risk assessment is spiropidion and its metabolites SYN547305, SYN547435, and SYN548430 (expressed as parent equivalents). For rotational crops, the residue definition for enforcement is spiropidion and its metabolite SYN549098 (free and conjugated; expressed as parent equivalents), while the residue definition for risk assessment is spiropidion and its metabolites SYN549098 (free and conjugated) and SYN550838, expressed as parent equivalents.

The data gathering and enforcement analytical methods are valid for the quantitation of residues of spiropidion, SYN547305, SYN547435, SYN548430, SYN549098 and SYN550838 in primary and secondary crops.

The combined residues of spiropidion and SYN547305 are stable in representative matrices from five commodity categories (high water (apple, radish leaves, spinach), high oil (soybean seed, cottonseed), high protein (dried bean), high starch (potato tuber, wheat grain, barley grain, radish roots) and high acid (orange)) for up to 24 months when stored at ≤-18°C, and stable for up to 18 months in carrot and processed commodities. Therefore, combined spiropidion residues are considered stable in all raw agricultural commodities (RACs), except carrot, for up to 24 months and in carrot and processed commodities for up to 18 months. Residues of SYN549098 are also stable in rotational crops (high starch (radish roots, wheat grain, carrot) and high water (radish leaves, spinach)) for up to 24 months of frozen storage.

Spiropidion residues concentrated in the following processed commodities: dried tomato (2.9-fold), citrus oil (73.3-fold), and raisins (2.1-fold). Residues of SYN547305 concentrated in the following processed commodities: potato flakes (3.49-fold), potato fries (1.43-fold), baked potato with skin (1.69-fold), soybean flour (1.6-fold), tomato paste (3.7-fold), tomato purée (1.7-fold), dried tomato (12.2-fold), dried apple (1.1-fold), orange peel (2.7-fold), grape juice (up to 1.5-fold), wine (up to 5.2-fold), and raisins (2.2-fold). Crop field trials conducted throughout Canada and/or the United States using end-use products containing spiropidion at approved rates in or on potatoes, leaf lettuce, head lettuce, spinach, mustard greens, broccoli, cabbage, cauliflower, Brussels sprouts, tomatoes, peppers, eggplants, cucumber, cantaloupe, summer squash, soybeans, orange, lemon, grapefruit, apple, pear, grape, and cottonseed are sufficient to support the proposed maximum residue limits (MRLs) or revise currently established MRLs.

Field rotational crop studies were conducted in/on mustard, lettuce, carrot, turnip and wheat matrices. The data are adequate to demonstrate that an immediate plant-back interval is

appropriate for labelled crops and a 30-day plant-back interval is appropriate for non-labelled crops.

3.5.2 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 years 2005-2010.

3.5.2.1 Acute dietary exposure results and risk characterization

The following refinements were applied to the acute analysis for spiropidion: highest average field trial (HAFT) residue values from the crop field trials and anticipated residues in processed commodities (where available). The refined acute dietary exposure (food alone) for all supported and imported spiropidion-treated food commodities is estimated to be 76% of the ARfD (0.03 mg/kg bw) for females 13–49 years old (95th percentile, deterministic), and up to 19% of the ARfD (0.30 mg/kg bw) for the remaining subpopulations. Aggregate exposure from food and drinking water (Level 1 EEC value = 33 µg a.i./L; surface water (daily)) is considered acceptable: 78% of the ARfD for females 13–49 years old, and 19% of the ARfD for the remaining subpopulations.

3.5.2.2 Chronic dietary exposure results and risk characterization

The following refinements were applied to the chronic analysis for spiropidion: supervised trial median residues (STMdR) from the crop field trials and anticipated residues in processed commodities (where available). The refined chronic dietary exposure (food alone) from all supported and imported spiropidion-treated food commodities for the total population, including infants and children, and all representative population subgroups is less than 19% of the acceptable daily intake (ADI; 0.03 mg/kg bw/day). Aggregate exposure from food and drinking water (Level 1 EEC value = 17 µg a.i./L; surface water (yearly)) is considered acceptable. The Health Canada estimates that chronic dietary exposure to spiropidion from food and drinking water is 8% of the ADI for the general population. The highest exposure and risk estimate is for children 1–2 years old (for < 1 year) at 20% of the ADI.

3.6 Aggregate exposure and risk assessment

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

As the risk estimated for each individual route of exposure is well below the level of concern, the aggregation of acute dietary and dermal exposures to spiropidion from pick-your-own activities is not of health concern.

Aggregation of chronic dietary (food and drinking water) and dermal exposures to spiropidion from harvesting, pruning, and thinning of pome fruit trees in residential settings was conducted. When combining dermal and dietary exposures and comparing the total exposure to the aggregate toxicological reference values, calculated MOEs were greater than the target MOE of

300 for adults and 100 for children (6 to < 11 years) (Appendix I, Table 10). As such, aggregate risks are not of health concern.

3.7 Exposure from drinking water

3.7.1 Concentrations in drinking water

For the human health risk assessment, estimated environmental concentrations (EECs) in potential drinking water sources were calculated for both groundwater and surface water. For drinking water, spiropidion was modelled as a combined residue with four of its transformation products (TPs; SYN547305, SYN548430, SYN548274, SYN548033) using the Pesticide in Water Calculator (PWC; version 3.0).

For surface water, 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 application timing, methods, and geographic scenarios, and are not considered conservative values that cover all regions of Canada.

Modelling was performed at Level 1. EECs in both surface water and groundwater were calculated for several scenarios representing different regions of Canada; only the highest EECs from across these scenarios are reported. All scenarios were run for 50 years. The major fate inputs for the drinking water modelling and the Level 1 drinking water EECs are presented in Tables 3.7.1.1 and 3.7.1.2, respectively.

Table 3.7.1.1 Major fate inputs for modelling EECs in drinking water.

Parameter	Drinking water	Details
K_d/K_{oc} (L/kg)	0.06/3.06	20th percentile of nine K_d values for the transformation product, SYN547305.
Water column metabolism half-life (day) at 20ºC	Stable	The aerobic aquatic whole system half-life of combined residue is stable.
Benthic metabolism half-life (day) at 20ºC	1000	Anaerobic aquatic whole system half-life.
Aqueous photolysis half-life (day) at 40°N	35	-

Parameter	Drinking water	Details
Hydrolysis half-life (day) at 25°C (pH 7)	Stable	-
Soil half-life (day) at 20°C	6.1	90% upper confidence bound on the mean of five soils.

Table 3.7.1.2 Level 1 EECs of combined residues of spiropidion and four of its TPs (in other words, SYN547305, SYN548430, SYN548274, SYN548033) 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]
3 × 200 g a.i./ha (7-day interval)	22	11	33	17	12

[1] Peak concentration.
[2] Post-breakthrough average concentration.
[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.

3.8 Cumulative assessment

The *Pest Control Products Act* requires the Agency 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 spiropidion.

Spiropidion acts to control insects by inhibiting acetyl-CoA carboxylase and interfering with lipid metabolism. Other insecticides with this same insecticidal mode of action include spirodiclofen, spiromesifen, spirotetramat, and spidoxamat. It is not known if these insecticides share the same mammalian mode of action. However, in the available mammalian toxicity studies, the thyroid gland was identified as a target tissue with four of these insecticides (spiropidion, spirodiclofen, spiromesifen, and spirotetramat) and effects on cholesterol metabolism, consistent with the insecticidal mode of action, were evident with three of these insecticides (spiropidion, spirodiclofen, and spiromesifen). Spidoxamat did not demonstrate these same effects (no thyroid effects or effects on cholesterol metabolism) in the toxicology database, and is not considered in this cumulative risk assessment.

Although adequate data are not available to establish the key events in the pathway that lead to the effects in the thyroid and on cholesterol metabolism, there was sufficient information to suggest a pattern of common effects across this structurally-related group of chemicals (tetronic and tetramic acid derivatives) that share an insecticidal mode of action. Based on the available information, it is not possible to rule out that spiropidion, spirodiclofen, spiromesifen, and spirotetramat share a common mode of action related to thyroid or cholesterol metabolism, and thus were considered at this time to form a common mechanism group (CMG). It is noted that the common toxic effects are only relevant to repeated exposure scenarios.

3.8.1 Human health reference values (HHRV) based on common effects observed in common mechanism group (CMG)

The above-noted common effects were not the most sensitive endpoints in the toxicology databases, as human health reference values were based on other endpoints such as reduced body weight or effects on other organs (brain, thymus, adrenal gland) that occurred at lower dose levels. For the purpose of the cumulative risk assessment, the lowest point of departure (POD) for the common effects was identified for each active ingredient in the CMG and compared to the existing human health reference values. When factoring in appropriate assessment factors, the human health reference values based on the lowest point of departure (POD) for the common effect compared to the existing reference values for the most sensitive endpoints are as follows:

- Spiropidion: 1.9-fold higher than the current ADI and the toxicology reference values for dermal and inhalation exposure scenarios involving adults; the existing toxicology reference value for dermal exposure scenarios involving children is based on a common endpoint.
- Spirodiclofen: 5.6-fold higher than the current ADI and the toxicology reference values for dermal and inhalation exposure scenarios.
- Spiromesifen: 2.9-fold higher than the current ADI and the toxicology reference values for dermal and inhalation exposure scenarios.
- Spirotetramat: 3.8-fold higher than the current ADI; the existing toxicology reference values for dermal and inhalation exposure scenarios are based on a common endpoint.

When assessing cumulative risk based on the common effect, these differences were used to adjust risk estimates of each active ingredient that were calculated with the existing toxicology reference values.

3.8.2 Exposure pathways and co-occurrence of exposure

Based on the uses and exposure pathways of spiropidion, spirodiclofen, spiromesifen, and spirotetramat (Table 3.8.2.1), there is a potential for co-occurrence of dietary and residential exposure for proposed and registered end-use products in this class of insecticides (including those with established Canadian maximum residue limits (MRLs) on imported food commodities). As such all four pesticides form the cumulative assessment group (CAG) and are included in the cumulative health risk assessment.

Table 3.8.2.1 Summary of uses and exposure pathways for registered and proposed tetronic and tetramic acid derivatives group of pesticides

Active ingredient	Health Canada published document	Pesticide uses	Potential exposure pathways		
			Food	Drinking water	Residential
Spiropidion	Current assessment and PMRL2023-02	Various crops including fruits (including pome) and vegetables, greenhouse vegetables and	Yes	Yes	Yes[1]

Active ingredient	Health Canada published document	Pesticide uses	Potential exposure pathways		
			Food	Drinking water	Residential
		imported food commodities			
Spirodiclofen	REG2006-06, PMRL2014-21, PMRL2014-41, EMRL2011-30	Pome fruit, stone fruit, tree nuts (crop group 14), grapes, hops, and highbush and lowbush blueberries	Yes	Yes	Yes[1]
Spiromesifen	RD2012-15 ERC2007-08, PMRL2023-32 PMRL2024-20	Various crops including greenhouse and outdoor ornamentals; field, vegetable and fruit crops	Yes	Yes	Yes[2]
Spirotetramat	PRD2008-07, PMRL2016-61, PMRL2017-31	Various crops including greenhouse and outdoor grown ornamentals, conifers, greenhouse vegetables and a variety of field, vegetable and fruit crops (including pome and stone fruit and tree nuts)	Yes	Yes	Yes[1,2]

[1] Residential exposure from treated residential orchard trees
[2] Residential exposure from use on residential ornamentals

3.8.3 Residential exposure

Residential exposure is expected from postapplication activities when residential pome and stone fruit trees are treated with spiropidion, spirodiclofen or spirotetramat by commercial applicators, as well as when ornamentals in residential areas are treated with spiromesifen or spirotetramat by commercial applicators.

It is not expected that a person would be conducting postapplication activities in treated ornamentals and in treated fruit trees each day for a short-term (less than 30 days) to intermediate-term (less than 90 days) basis. In addition, it is not expected that the same residential trees and ornamentals would be treated with two or more of these pesticides, as they have the same mode of action and labels recommend rotation with insecticides with other modes of action. As such, only the residential exposure scenario that results in the highest exposure and risk was included in the calculation of cumulative health risk estimates for this CAG.

The most recent residential risk assessments for spiropidion, spirodiclofen, spiromesifen and spirotetramat were considered and risk estimates were adjusted for the difference between the human health reference values of the common effect and the established toxicology reference values for dermal exposure. Out of all the residential exposure scenarios of all four active ingredients, postapplication exposure from ornamental gardens treated with spiromesifen yielded the highest risk estimates based on the common effect of the CAG.

The risk assessment was conducted following the 2012 USEPA Residential SOP under Section 4: Garden and Trees for the registered use of spiromesifen on outdoor ornamentals. Using the established dermal toxicology reference value (TRV) for spiromesifen (NOAEL of 2.2 mg/kg bw/day, target MOE of 300; PRD2011-09), the calculated MOE was 525 and 768 for adults and children 6 to <11 years old, respectively, which corresponds to 57% and 39% of the risk cup. However, the established dermal TRV is based on different effects (spleen and thymus effects) compared to the common effects associated with this CAG (effects in the thyroid and on cholesterol metabolism), which were seen at 6.3 mg/kg bw/day. As such, to take this 2.9-fold difference into account, the percent risk cup based on the common effects would be 20% and 14% for adults and children 6 to <11 years old, respectively.

3.8.4 Dietary exposure

As noted above, the common toxic effects in the CAG are only relevant to repeated exposure scenarios. As such, to assess cumulative dietary risk, only chronic exposure was considered. The most recent chronic dietary (food and drinking water) exposure assessments (DEAs) of spiropidion, spirodiclofen, spiromesifen and spirotetramat are summarized in Appendix I, Table 11, all of which were refined. As mentioned above, the common effects of the CAG (effects in the thyroid and on cholesterol metabolism) were not the most sensitive endpoints in the toxicology databases, as human health reference values were based on other endpoints such as reduced body weight or effects on other organs (brain, thymus, adrenal gland) that occurred at lower dose levels. As such, to assess cumulative dietary risk, the risk estimates from the most recent DEAs of the individual active ingredients were adjusted by the difference between the human health reference value based on the common effect and currently established ADI.

To estimate the cumulative dietary risk of this CAG, the adjusted risk estimates of spiropidion, spirodiclofen, spiromesifen and spirotetramat were summed for all subpopulations (Appendix I, Table 12) with the highest exposed subpopulation being children 1–2 years old (37.3% of the risk cup). This additive approach is considered a likely overestimation of potential exposure as it assumes full co-occurrence of food residues.

3.8.5 Aggregate exposure

To take into account residential exposure, a simple sum of the adjusted dermal risk estimates (20% and 14% of the risk cup for adults and children 6 to <11 years old, respectively, from postapplication exposure from ornamental gardens treated with spiromesifen) and the cumulative dietary risk estimates (17.1% and 18.4% of the risk cup for adults 50+ years old (highest exposed adult population) and children 6–12 years old) was calculated for the relevant subpopulations. As such, aggregate cumulative risk for children (6 to <11 years) and adults were 37% and 32% of the risk cup, respectively.

Since these cumulative risk estimates are below 100% of the risk cup, the cumulative risks from potential non-occupational co-exposure to spiropidion, spirodiclofen, spiromesifen, and spirotetramat through food, drinking water and residential exposure, where relevant, are acceptable.

3.9 Maximum residue limits

Dietary risks from the consumption of food commodities listed in Table 3.9.1 were shown to be acceptable when spiropidion is used according to the supported label directions. Therefore, foods containing residues at these levels are safe to eat, and Health Canada recommends that the following MRLs be specified for residues of spiropidion.

Table 3.9.1 Recommended maximum residue limits

MRL (ppm)	Food commodity
100	Citrus oil
15	Leafy vegetables (crop group 4-13), except watercress; Brassica head and stem vegetable (crop group 5-13), except Brussels sprouts
5	Wine
4	Raisins
3	Oranges (Revised) (crop subgroup 10A); fruiting vegetables (crop group 8-09)[1]
2	Small fruit vine climbing, except fuzzy kiwifruit (crop subgroup 13-07F); Brussels sprouts
1.5	Tuberous and corm vegetables (crop subgroup 1C)[2]; cucurbit vegetables (crop group 9)[3]
0.9	Lemons/limes (Revised) (crop subgroup 10B)
0.6	Pome fruit (crop group 11-09); cottonseeds (Revised) (crop subgroup 20C)
0.4	Grapefruits (Revised) (crop subgroup 10C)

[1] The proposed MRL for CG 8-09 (fruiting vegetables) is intended to replace the established MRLs of the individual crops, tomatoes, bell peppers, non-bell peppers, and tomato paste.

[2] The proposed MRL for CSG 1C (tuberous and corm vegetables) is intended to replace the established MRL for potato.

[3] The proposed MRL for CG 9 (cucurbit vegetables) is intended to replace the established MRLs of the individual crops, cantaloupe, muskmelons, pumpkins, watermelons, winter squash, and cucumbers.

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 maximum residue limits (MRLs) in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in plant matrices, analytical methodologies, field trial data, and acute and chronic dietary risk estimates are summarized in Tables 13, 14 and 15 in Appendix I.

3.10 Health incident reports

As of 15 December 2025, no human or domestic animal incidents involving the active ingredient spiropidion have been submitted to Health Canada.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

A summary of the major transformation products (TPs) for spiropidion is provided in Appendix I, Table 16. The environmental fate parameters for spiropidion and its major TPs are provided in Appendix I, Table 17.

Terrestrial environment:

The main dissipation pathways for spiropidion in the terrestrial environment are hydrolysis and biotransformation in soil. Phototransformation on soil is negligible.

The rate of hydrolysis for spiropidion is temperature and pH dependent. Hydrolysis is fastest at pH 9 and slower at pH 4 and 7. The rate of hydrolysis increases with temperature. Spiropidion is hydrolyzed to the major TP, SYN547305.

Biotransformation in soil is a major route of transformation for spiropidion. It is non-persistent in aerobic and anaerobic soil, with half-lives (DT_{50} values) ≤1.1 days. Two major TPs, SYN547305 and SYN552257, were identified from the biotransformation of spiropidion in aerobic soils and two major TPs, SYN547305 and SYN548430, were identified in anaerobic soil. Both SYN547305 and SYN552257 are non-persistent to slightly persistent in aerobic soils (DT_{50} values 0.13 to 34 days) while SYN547305 is persistent in anaerobic soils (DT_{50} values of 165 to 839 days). Information regarding the persistence of SYN548430 in anaerobic soil is not available because its concentration was still increasing at the end of the study.

Three terrestrial field dissipation (TFD) studies on bare soil were conducted in three ecoregions relevant to Canada. spiropidion dissipated rapidly after application at all three sites and was not measured above the limit of quantification (LOQ) of 1 part per billion (ppb) between 8 and 60 days after the last application. Up to nine TPs (SYN547305, SYN548033, SYN549098, SYN549979, SYN548037, SYN548430, SYN550839, SYN552045 and SYN552257) were included in the chemical analysis for the TFD studies and were measured in soil samples. Of these, two TPs, SYN547305 and SYN548033, were measured at >10% of applied spiropidion. Spiropidion and its TPs all dissipated rapidly; half-life (DT_{50}) values based on the combined residue of all analytes were less than five days. After one year, the residues of spiropidion and all of its TPs in the field were <2% of the total applied amount of spiropidion. As such, carryover of spiropidion residues into the next growing season is not expected to be a concern.

Spiropidion was observed to have moderate to high mobility in soils tested in the laboratory, while its TPs had high to very high mobility. No significant downward migration of spiropidion and its TPs was observed in the field, with the majority of residues remaining in the top 10 cm of soil; however, water input at two of the three field sites may have been insufficient to adequately assess leaching. Based on the available weight-of-evidence (mobility information, leaching criteria of Cohen et al., (1984), groundwater ubiquity scores (GUS), and groundwater

modelling), leaching of spiropidion residues to groundwater may be a concern. Based on this information, and because SYN547305, SYN548430, SYN548274 and SYN548033 are included in the residue definition for drinking water, a precautionary label statement is proposed to inform users to avoid use of A20262 Insecticide in areas where the soils are permeable, particularly where the water table is shallow.

Aquatic environment:

Spiropidion residues are broken down in water via the combined processes of hydrolysis, phototransformation and biotransformation. As noted above, hydrolysis is an important transformation process for spiropidion, particularly under alkaline conditions (pH 9), such as those found in the marine environment. Aqueous phototransformation is a negligible process for spiropidion; however, under irradiated conditions, SYN547305 is transformed into SYN548274 by oxidative dechlorination, followed by cleavage to SYN551480.

Spiropidion is non-persistent in aerobic and anaerobic aquatic systems, with half-lives in the total system (water and sediment) of less than three days. The biotransformation of spiropidion in aquatic systems resulted in the production of two major TPs, SYN547305 and SYN548430, in the water and sediment of all tested systems. SYN547305 is persistent in the tested systems, while data were not available to determine the persistence classification for SYN548430. Some spiropidion rapidly partitioned from water to the sediment phase on Day 0 in both aerobic and anaerobic systems (<20% of applied radioactivity (AR)); however, spiropidion and its TPs were mainly measured in the water phase (>70% AR). Significant accumulation of spiropidion and its TPs in sediment is not expected.

The log K_{ow} value of 3.3 for spiropidion indicates the potential to bioaccumulate while the log K_{ow} values for SYN547305 (2.54 at pH 5 to -0.22 at pH 9) and SYN548430 (<1 at pH 5 to 9) do not. A study evaluating the bioconcentration of spiropidion in bluegill sunfish was submitted. Spiropidion was observed to be unstable in the test system, resulting in the formation of SYN547305. As such, bioconcentration factors were determined based on the combined residue of spiropidion and SYN547305 (in parent equivalents). The study showed that spiropidion and SYN547305 had low potential to bioconcentrate in fish, with bioconcentration factors <55. The residues were rapidly eliminated from fish, with 96% depuration after five days.

Atmospheric fate:

Spiropidion and its major TPs, with the exception of SYN548037, have low vapour pressures and low Henry's law constants, which indicate a low potential for volatilization in the field. SYN548037 has intermediate to high volatility based on its vapour pressure; however, it is very soluble in water and it is not expected to be volatile from a water surface or moist soil based on its Henry's law constant. This is supported by the laboratory fate studies which did not find significant amounts of radioactivity in the organic traps to collect volatile compounds.

4.2 Environmental risk characterization

An environmental risk assessment was conducted as described in the Health Canada 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 estimated environmental

concentrations (EECs) to effects-based values used to assess risk (effects metrics). The EECs are estimated using standard models considering application rate(s), and chemical and environmental fate properties, including the dissipation of the pesticide between applications. The EECs used in the risk assessment are presented in Appendix I, Table 18.

Acute and chronic ecotoxicological data for non-target terrestrial, freshwater and marine organisms were submitted by the applicant and 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 evaluated additional and more realistic exposure scenarios, including consideration of spray drift and runoff as well as effects metrics that were more reflective of potential exposure in the environment. Refinements to the risk assessment continued until the risk was adequately characterized or the available data did not permit further refinements.

4.2.1 Risks to terrestrial organisms

Terrestrial organisms, such as earthworms, bees and other beneficial arthropods, birds, wild mammals and non-target terrestrial plants may be exposed to spiropidion through direct contact with spray or spray drift, contact with sprayed surfaces or from ingestion of contaminated food. A risk assessment for spiropidion, its major TPs and the end-use product, A20262 Insecticide, was undertaken based on available toxicity data.

The screening level risk assessment for terrestrial organisms, with the exception of birds and mammals, is shown in Appendix I, Table 20. At the screening level, the EEC for spiropidion in soil was calculated based on a direct overspray of the maximum cumulative application rate based on three applications of 200 g a.i./ha, with a re-application interval of 7 days and a half-life in aerobic soil of 1.48 days (90% upper confidence bound on the mean of five available values). Soil EECs were converted from g a.i./ha to mg a.i./kg using the assumption that spiropidion is homogeneously mixed in the top 15 cm soil layer with a soil bulk density of 1.5 g/cm^3. EECs on plant surfaces in the field were calculated using the same application rate but with a default foliar half-life of 10 days.

The EECs for the major TPs were conservatively calculated based on the maximum spiropidion application rate (three applications of 200 g a.i./ha), assuming 100% conversion of the parent on a molar basis. No dissipation of the parent or TP between applications was considered.

Earthworms

Earthworms could be exposed to spiropidion when it is applied to crops, resulting in soil exposure. Acute and chronic toxicity data for earthworms are available for spiropidion and the major TPs produced in soil (SYN547305, SYN548033, SYN552045 and SYN552257), with the exception of SYN548037. In the phototransformation on soil laboratory study, SYN548037 was produced only in moist soil under irradiated conditions at a maximum mean of 10.7% AR via the transformation of SYN547305; however, it was measured at <1% of the total applied amount in the terrestrial field dissipation studies. As such, significant environmental exposure to this TP in the field is not expected and an earthworm toxicity test was not required.

The screening level RQs for earthworms were below the LOC of 1 (Appendix I, Table 20). As such, risks to earthworms are acceptable.

Beneficial arthropods

Soil dwelling beneficial arthropods could be exposed to spiropidion when it is applied to crops, resulting in soil exposure. Foliar-dwelling beneficial arthropods could also be exposed to spiropidion spray droplets during application and to residues on plant surfaces. Toxicity tests for beneficial arthropods were conducted with the formulated product, A20262B Insecticide (301 g a.i./L), as well as the TP, SYN547305, which has a similar toxicity to terrestrial invertebrates as spiropidion.

A LOC of 1 was used in the screening level risk assessment of beneficial arthropods, with the exception of the predatory mite (*Typhlodromus pyri*) and the parasitic arthropod (*Aphidius rhopalosiphi*). For these species, the screening level risk assessment used a LOC of 2 when considering endpoints derived from spray application on glass plates. Significant ecological effects for these species at the population level are not expected to occur below the LOC of 2 based on an extensive empirical comparison of the risk quotients and known acceptable effects from field and semi-field studies for these two indicator species.

The screening level RQs for beneficial arthropods were below the LOCs, with the exception of the RQ of <1.5 for the ladybird beetle, which is based on a non-definitive endpoint (Appendix I, Table 20). This endpoint was derived from a limit toxicity test where no adverse effects were observed at the tested concentration of 270 g a.i./ha. As such, the use of this endpoint to assess risk to the ladybird beetle overestimates risk.

To further characterize the potential risk to the ladybird beetle, off-field spray drift was considered assuming spray drift factors of 6% for field sprayer (based on medium spray droplet classification, as required by the label), and 74% for early season airblast. The spray drift factor is defined as the maximum percentage of spray drift deposition at one metre downwind from the point of application. The off-field RQs were <0.09 and <1.1 for spray drift from field sprayer and early season airblast applications, respectively (Appendix I, Table 21). Due to the limited effects off-field, it is expected that populations will move on-field and repopulate.

When considering the available weight-of-evidence: (1) on-field RQs below the LOCs for most beneficial arthropods, (2) the use of an effects metric that overestimates toxicity to the ladybird beetle (in other words, a non-definitive endpoint), and (3) off-field RQs for the ladybird beetle were below, or slightly exceeding, the LOC of 1, risks to beneficial arthropods are acceptable.

Bees

Foraging bees may be exposed to spiropidion spray droplets during application (contact exposure) or through ingestion of spiropidion residues in pollen and nectar (oral exposure). Additionally, immature and adult bees inside colonies may be exposed to spiropidion residues if foraging bees bring contaminated pollen and nectar back to the hive. Spiropidion is systemic and translocates in both the phloem and xylem of a plant's vascular system, resulting in residues moving throughout the plant when it is sprayed. It also quickly transforms to SYN547305 after application.

Acute and chronic laboratory toxicity tests for adult and larval honey bees are available for spiropidion and SYN547305; acute bumble bee toxicity tests (contact and oral exposure) for spiropidion are also available. Spiropidion and SYN547305 are classified as practically non-toxic to adult bees on an acute basis; however, adverse effects on survival were observed in the larval toxicity and adult chronic toxicity laboratory tests.

The screening level risk assessment for pollinators considers conservative toxicity endpoints from laboratory studies. It also uses the maximum single application rate (in other words, 200 g a.i./ha) to estimate the highest potential exposure. This is considered to be conservative because individual flowers generally only bloom for a short period of time and it is unlikely that the same forager bee would be exposed to a flower that was sprayed with spiropidion multiple times.

In the screening level risk assessment, acute risks to adult honeybees and bumblebees from oral and contact exposure are acceptable (in other words, RQs are below the LOCs of 0.4 for acute exposure and 1 for chronic exposure); however, some of the RQs for honey bee larvae and for adult honey bee chronic oral exposure exceed the LOCs for both spiropidion and SYN57305. Maximum RQs of 32 and 10, based on dose per bee and concentration in diet, respectively, were calculated for 4-day larval repeat exposure to SYN547305 (Appendix I, Table 20).

Given the exceedances of the LOCs at the screening level, risks to larval and adult bees were further characterized using a weight-of-evidence approach considering the following lines of evidence:

- The use of measured pollen and nectar concentrations from field residue studies to refine the screening level (Tier 1) RQs. The relevance of the field residue studies to the Canadian use pattern was taken into consideration in the risk assessment.
- Consideration of the results of semi-field (tunnel) and colony feeding studies (Tier II).
- Consideration of crop attractiveness to bees.

Studies evaluating the residues of spiropidion and SYN547305 in field crops (cucumber, dry bean, apple, tomato and potato) following application of formulated spiropidion products at different application rates and timings were submitted. At least one application of spiropidion was made during bloom, with the exception of some of the cucumber trials where spiropidion was applied before bloom. The studies showed that spiropidion and SYN547305 concentrations in pollen and nectar are highest when crops are sprayed during bloom and then generally decrease between applications; however, residues in pollen and nectar are measurable even when the crops are sprayed prior to bloom (Appendix I, Table 22). As such, bees may be exposed to

spiropidion and SYN547305 in pollen and nectar, even if flowers are not present when the plant is sprayed.

The screening level RQs were refined based on the measured combined residue of spiropidion and SYN547305 in pollen and nectar from the field crops. The combined residue was used because of the rapid transformation of spiropidion to SYN547305, which exhibits higher chronic toxicity to bees than spiropidion. The sampling interval with pollen and nectar concentrations resulting in the highest EECs were selected for use in the risk assessment. The effects metrics used to calculate refined screening level RQs were based on SYN547305 endpoints.

The refined screening level EECs and RQs based on dose per bee and concentration in diet are presented in Appendix I, Tables 23 and 24, respectively. When spiropidion was applied to cucumber crops prior to bloom, the RQs were below the LOCs; however, LOC exceedances for at least one of single larval exposure (acute), repeat larval exposure (chronic) or adult chronic oral exposure occurred for all other crops when at least one application of spiropidion was made during bloom. The maximum RQs were for chronic larval exposure based on the concentrations of spiropidion residues in pollen and nectar of apple crops (29 and 9.2 on a dose and concentration in diet basis, respectively).

Given that the RQs continued to exceed the LOCs based on field residue data, the results of two semi-field and two colony feeding studies were also considered. The studies are summarized in Appendix I, Table 25. The semi-field (tunnel studies), which included application of spiropidion while bees were actively foraging, did not show adverse effects on survival or colony health at application rates of 2 x 300 g a.i./ha or 3 × 180 g a.i./ha; however, a reduction in flight activity was observed on the day of application in one study. The bees appeared to recover from this effect by the next day. Short-term oral exposure (<72 hours) to spiropidion via in-hive sucrose feeding did not cause adverse effects in colonies exposed to spiropidion concentrations up to 32 ppm (mg a.i./kg sucrose solution); however, longer-term (6-week) sucrose feeding at 50 ppm resulted in decreased colony health. A statistically significant effect on colony survival rates was not observed; however, survival of the hives treated with spiropidion was lower than the controls. All of the control hives survived the winter while 75, 83 and 75% of the hives in the 12.5, 25 and 50 ppm treatments, respectively, survived. It is unclear if exposure to spiropidion played a role in the colony deaths since statistically significant effects were not observed.

A no-observed-adverse-effect-level (NOAEL) and lowest-observed-adverse-effect level (LOAEL) of 25 and 50 ppm, respectively, were derived from the 6-week colony feeding study. The LOAEL is associated with statistically significant reductions in colony strength, pupae, total brood, nectar and pollen stores compared to the controls.

In order to estimate colony level risk, the RQs were further refined by comparing the sampling interval with the highest mean concentration of spiropidion residues in nectar and pollen to the NOAEL and LOAEL from the 6-week colony feeding study (Appendix I, Table 26). When considering the NOAEL, the RQs based on nectar concentrations were all below the LOC of 1; however, RQs based on pollen concentrations exceeded the LOC of 1 for the cucumber, apple and tomato crops when at least one application of spiropidion was made during bloom (RQs of 1.7, 15 and 1.2, respectively). When considering the LOAEL, the RQs were below the LOC of 1, with the exception of the RQ of 7.5 for apple pollen following two application of 300 g a.i./ha, with the first application before bloom and the second at early bloom.

In order to bracket the risk estimates, RQs were further refined for crops with LOC exceedances based on the NOAEL or LOAEL (cucumber, apple and tomato) by considering pollen data from sampling intervals after those that produced the highest mean pollen concentrations (Appendix I, Table 26). This was continued until the RQ was below the LOC or residue data were no longer available. When considering pollen concentrations from additional sampling intervals, the RQs for cucumber and tomato based on the NOAEL were below the LOC by 5 to 6 days after the third spiropidion application (DAA3). The RQs for apple slightly exceeded, or were equal to, the LOC for all available sampling intervals (RQs ≤ 1.2) when considering the NOAEL; risks were acceptable based on the LOAEL.

The above RQs demonstrate that adverse effects to bee colonies may occur from chronic exposure to spiropidion when it is applied during bloom at concentrations similar to those expected in the field; however, there are uncertainties with the risk estimates. The uncertainties in the risk assessment are outlined in Appendix I, Table 27. Mitigation is required to reduce the exposure of bees to spiropidion residues in pollen and nectar. Crop attractiveness to bees was considered when determining risk mitigation measures.

In Canadian field crops, spiropidion is proposed for use on leafy vegetables (for example, lettuces and herbs), brassica head and stem vegetables (for example, broccoli, cauliflower), fruiting vegetables (for example, eggplant, tomato), cucurbit vegetables (for example, cucumber, squash and melons), pome fruits (for example, apple and pear) and grapes. In greenhouse crops, it is proposed for use on tomatoes, peppers, eggplant and cucumbers. These crops have varying degrees of attractiveness to bees. Bee exposure from leafy vegetables and brassica head and stem vegetables, which are generally harvested prior to bloom, is expected to be limited. Fruiting vegetables are moderately attractive to bees while cucurbit vegetables and pome fruit are highly attractive to bees. Grapes self pollinate and have negligible/low attractiveness to bees.

Given that spiropidion is systemic, the pollen and nectar of crops that are not harvested prior to bloom (fruiting vegetables, cucurbit vegetables, pome fruit and grapes) may contain residues even if spiropidion is applied pre-bloom; however, the RQs based on the field residue studies where spiropidion was applied to cucumber crops pre-bloom were below the LOCs. Additionally, cucurbits flowers only last for one day and close in the evening. Therefore, application to cucurbit crops during bloom in the evening after flowers close is expected to result in minimal exposure to residues from direct spray to nectar and pollen.

The following mitigation measured are required to decrease pollinator exposure to spiropidion and SYN547305:

- Label statements advising users that spiropidion is toxic to bees.
- Prohibition on the application of spiropidion to highly bee attractive field crops (pome fruit) during bloom.
- Application of spiropidion to fruiting vegetables and cucurbit vegetables is restricted to the evening when plants are in bloom.
- Label statements advising users that spiropidion may harm brood of bees used in greenhouse production and that application should be avoided when bees are in the treatment area.

Terrestrial vertebrates – Birds and wild mammals

A screening level risk assessment was conducted to evaluate acute and reproductive risks to birds and mammals based on the estimated concentration of spiropidion in various food items in the diet (the estimated daily exposure (EDE)). Exposure is dependent on the body weight of the organism, and the amount and type of food consumed. As such, a set of generic body weights was used to represent a range of species (20, 100, and 1000 g for birds and 15, 35, and 1000 g for mammals), and specialized feeding guilds (in other words, herbivore, frugivore, insectivore and granivore) were considered for each category of animal weights.

The screening level risk assessment evaluated a conservative exposure scenario based on:

- The maximum spiropidion residue concentrations in food items;
- A diet that is composed entirely (100%) of a particular, spiropidion-contaminated food item; and,
- The feeding guild assumed to have the highest exposure for each animal weight category.

If a concern was identified at the screening level (in other words, RQ > LOC of 1), the risk was then further characterized.

Based on the screening level risk assessment, acute risks to birds and wild mammals from the use of spiropidion are acceptable (RQs <0.4; Appendix I, Table 28). The RQs for reproductive risk for small and medium sized birds and medium sized mammals slightly exceeded the LOC (RQs ≤ 1.6). As such, reproductive risks for these groups were further characterized by expanding the assessment to include all relevant food guilds and considering both on-field and off-field maximum and mean residues values (Appendix I, Tables 29 and 30).

The on-field reproductive RQs for small, insectivorous birds (RQ = 1.6), medium sized insectivorous birds (RQ = 1.3) and medium sized herbivorous mammals (RQs ≤ 1.5) exceeded the LOC based on maximum residues. The on-field RQs based on mean residues were below the LOC, with the exception of the RQ of 1.1 for small, insectivorous birds.

Off-field EECs were determined based on spray drift of spiropidion one-metre downwind from the point of application. Spray drift factors of 6% and 74% for field sprayer (medium spray droplet) and early season airblast application, respectively, were used to calculate off-field EECs. When considering the maximum residue values, all off-field reproductive RQs were below the LOC, with the exception of the off-field RQs for small insectivorous birds (RQ = 1.2) and medium sized herbivorous mammals (RQs ≤ 1.1) exposed to spray drift from early season airblast. Off-field RQs considering mean nomogram residues were below the LOC.

Reproductive risks were estimated based on no-observed effect dose (NOED) values. In order to further characterize the risks, the lowest-observed effect doses (LOED) from the studies were also considered.

- For birds, the NOED of 20 mg a.i./kg bw/d was determined from a reproductive toxicity test with the mallard duck. The LOED from this study was 60 mg a.i./kg bw/d, based on a 20% reduction in reproduction. When considering the LOED, RQs were below the LOC for birds on-field and off-field (Appendix I, Table 31).

- For mammals, the NOED of 24 mg a.i./kg bw/d was determined from a two-generation rat reproductive toxicity test. No effects on reproduction were observed up to the highest doses tested (in other words, 300 ppm (equivalent to 24 mg a.i./kg bw/d) for females and 500 ppm for males). A LOED is not available. Adverse effects to mammals are not expected from the proposed use of spiropidion given that the maximum RQ of 1.1 for medium sized herbivorous mammals only slightly exceeded the LOC of 1 based on a NOED value.

The RQs were calculated assuming that the diet of birds and mammals would be composed 100% of food items contaminated with spiropidion for multiple days. However, diets are likely to be composed of both contaminated and uncontaminated food items. Furthermore, the concentration of spiropidion residues in food items are expected to be highest immediately after application and then decrease thereafter. When considering the available weight-of-evidence (slight exceedances of the LOC of 1 when RQs are based on NOED values (RQs ≤ 1.6), RQs below the LOC when based on LOED values, low likelihood of a diet composed 100% of contaminated food items, off-field risks based on mean residues were below the LOC), risk to birds and mammals are considered to be acceptable.

Non-target terrestrial plants

The screening level risk assessment for non-target terrestrial plants considered risk due to a direct overspray of spiropidion. Toxicity studies investigating the effect of the spiropidion end-use product, A20262B, on seedling emergence and vegetative vigour are available. The RQ for seedling emergence was below the LOC; however, the RQ of 2.6 for vegetative vigour was not (Appendix I, Table 20). As such, the risk assessment was further refined to consider off-field spray drift of spiropidion one-metre downwind from the point of application (6% and 74% spray drift for field sprayer and early season airblast, respectively).

The off-field RQ based on 6% spray drift from field sprayer was below the LOC; however, the RQ for 74% spray drift for early season airblast exceeded the LOC (Appendix I, Table 21). Spray buffer zones to protect sensitive terrestrial habitat off-field were calculated based on the maximum application rate for each crop. Spray buffer zones of up to 2 metres are required on the label of A20262 Insecticide to protect sensitive terrestrial habitat. With the inclusion of the spray buffer zones, risks to non-target terrestrial plants are acceptable.

4.2.2 Risks to aquatic organisms

Aquatic organisms, such as invertebrates, fish, amphibians and aquatic plants could be exposed to spiropidion if spray drift or runoff enter aquatic habitats. In the screening level risk assessment, EECs were calculated as follows:

- The EECs for spiropidion in surface water were calculated based on a direct overspray to a one-hectare wetland at the cumulative application rate of three applications of 200 g a.i./ha with a re-application interval of 7 days and a half-life of 2.60 days in water.
- EECs for the major TPs (SYN547305, SYN548033, SYN48274, SYN548430, SYN551480, SYN552045, and SYN552257) were each calculated assuming 100% transformation of spiropidion to each TP on a molar basis. No dissipation of the parent or TPs between applications was considered.

Water bodies of two different depths were evaluated: an EEC in surface water 15 cm deep was used to determine risk to amphibians while an EEC at an 80 cm depth was used to evaluate risks to all other aquatic organisms.

Spiropidion is classified as moderately to highly toxic to freshwater and estuarine/marine aquatic organisms (Appendix I, Table 19). Available data show that the major TPs are less toxic than spiropidion. Spiropidion and its TPs are expected to mainly be found in the water phase of aquatic systems based on the results of the environmental fate studies. Two 10-day studies evaluating the toxicity of spiropidion-spiked sediments to the freshwater invertebrates, *Hyalella azteca* and *Chironomus dilutus*, were used to evaluate risks to benthic species.

In the screening level risk assessment (Appendix I, Table 32), risks to non-target pelagic and benthic aquatic organisms from exposure to spiropidion and its TPs were acceptable, with the exception of acute and chronic risks to amphibians (RQs ≤ 2.8) and chronic risks to marine invertebrates (saltwater mysid; RQ = 2.0) and estuarine/marine fish (sheepshead minnow; RQ = 1.2).

Applying spiropidion directly to water, as assumed in the screening level risk assessment, is not permitted. To further characterize risk to amphibians, estuarine/marine invertebrates and estuarine/marine fish, exposure to spiropidion via spray drift and runoff was considered.

Spray drift to freshwater

In order to evaluate risks from spray drift to off-field amphibian habitat, the aquatic EEC in 15-cm deep water was adjusted to account for deposition of spray drift one metre downwind from the point of application. Spray drift factors of 6% and 74% for application via field sprayer (medium sized spray droplets) and early season airblast, respectively, were used to calculate the off-field EEC.

The off-field RQs for amphibians exposed to spray drift from field sprayer application are below the LOC; however, the off-field RQs from airblast slightly exceeded the LOC (RQs ≤ 2.1; Appendix I, Table 33). Spray buffer zones up to one metre are required to protect sensitive freshwater habitats. With the inclusion of the spray buffer zones, risks to non-target freshwater organisms from spray drift are acceptable.

Spray drift to estuarine/marine environments

Estuarine and marine environments are dynamic systems characterized by tidal action. The size of estuaries can vary greatly. To ensure that the estuarine/marine risk assessment is protective of small, salt marshes as well as larger estuarine and marine environments, off-field EECs were calculated assuming spray drift to a 1-ha, 80-cm deep water body located 1-metre downwind from the point of applications. Given that small, salt marshes are expected to be flushed/recharged by tidal action, spray drift from multiple applications of spiropidion are not expected to accumulate in the water body due to tidal action. As such, EECs for spray drift to the estuarine/marine environment are calculated considering spray drift from only one application of spiropidion.

Chronic RQs for the saltwater mysid and the sheepshead minnow exceeded the LOC in the screening level risk assessment; acute risks to these organisms from spray drift are acceptable.

Chronic exposure is not expected to occur due to spray drift from a single application of spiropidion. As such, a spray buffer zone for the estuarine/marine environment is not required.

Runoff to aquatic habitat

EECs for spiropidion residues in surface water from runoff were modelled using PWC version 3.0. The PWC model calculates the amount of spiropidion entering a water body via runoff only, and its subsequent degradation in the water and sediment. The EECs were calculated by modelling a 10-ha field adjacent to 1-ha water bodies of two different depths: 15 and 80 cm. The model was run for 50 years. Several representative scenarios were modelled for different regions of Canada. The runoff EECs, along with the fate parameters used in the modelling, are presented in Appendix I, Table 34.

The results of the refined runoff risk assessment are summarized in Appendix I, Table 35. The maximum EECs, which were modelled for the scenario where three applications of 180 g a.i./ha were applied to pumpkin in Prince Edward Island with a 7-day interval, were used in the risk assessment. The maximum 24-hour and 21-day EECs were used to calculate acute and chronic risks, respectively. The acute RQ of 1.8 for amphibians slightly exceeded the LOC of 1, while the chronic RQs for amphibians, saltwater mysids and sheepshead minnow were below the LOC.

There are a number of conservative assumptions in the water modelling that overestimate risk. The modelling assumed that spiropidion would be applied at the maximum application rate for each crop. Only the highest EECs for all of the modelled scenarios were reported and used in the risk assessment. When considering the conservative assumptions used in the water modelling process, risks to aquatic organisms from runoff are acceptable when label directions, which include precautionary label statements to mitigate runoff, are followed.

4.2.3 Incident reports

As of 15 December 2025, no environmental incident reports have been submitted to Health Canada.

5.0 Value

In support of the value of A20262 Insecticide, reports from a total of 84 efficacy trials which were conducted between 2014 and 2022 were reviewed. These trials were conducted in 14 different countries (Australia, Brazil, Canada, Egypt, Germany, Greece, Hungary, Italy, Japan, South Africa, Spain, Turkey, USA, and Vietnam) on various crops including fruiting vegetables, cucurbit vegetables, leafy vegetables, brassica head and stem vegetables, pome fruit, grapes, and greenhouse tomatoes, peppers, eggplant and cucumber. Trials included assessments of the efficacy and/or phytotoxicity of A20262 Insecticide when applied as a foliar spray.

The efficacy trials demonstrated that A20262 Insecticide provides control of aphids, whiteflies, two-spotted spider mites, and/or mealybugs on all listed crops, except aphids on pome fruits, which has a claim of suppression. The value information supported the application of A20262 Insecticide with MSO adjuvant and demonstrated that in many cases, higher application rates provided improved or quicker control.

Aphids, whitefly, and two-spotted spider mites are common pests, and as a result, many products with a wide variety of active ingredients, including one other group 23 insecticide, spirotetramat, are registered for control of these pests on the listed crops. For mealybugs in grapes, registered active ingredients are spirotetramat, potassium salts of fatty acids, canola oil, malathion and clothianidin. A20262 Insecticide provides a new active ingredient for use against these pests and may contribute to resistance management by providing a new alternative which can be used in rotation with existing products. Group 23 insecticides are not known to have cross-resistance with other insecticide groups.

The value information was sufficient to support a claim that A20262 Insecticide will provide control or suppression of aphids, whitefly, two-spotted spider mite, and/or mealybugs on listed crops when applied at the labelled application rate with MSO adjuvant. Details of the supported uses are found in Appendix 1, Table 36.

6.0 Pest Control Product Policy considerations

6.1 Assessment of the active ingredient under the Toxic Substances Management Policy

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

During the review process, Spiropidion Technical Insecticide and its transformation products were assessed in accordance with Regulatory Directive DIR99-03[7] and evaluated against the Track 1 criteria. Health Canada has reached the conclusion that Spiropidion Technical Insecticide and its transformation products do not meet all of the TSMP Track 1 criteria.

Please refer to Appendix I, Table 37 for further information on the TSMP assessment.

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.[8] The list is used as described in Science Policy Note SPN2020-01[9] and is based on existing policies and regulations, including the Toxic Substance Management Policy and *Formulants Policy*,[10] and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives*

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

8 SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.

9 Science Policy Note SPN2020-01, Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under paragraph 43(5)(b) of the Pest Control Products Act

10 DIR2006-02, Formulants Policy and Implementation Guidance Document

Regulations under the *Canadian Environmental Protection Act, 1999*, (substances designated under the *Montreal Protocol*).

Health Canada has reached the conclusion that Spiropidion Technical Insecticide does 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*. Its end-use product, A20262 Insecticide, has, as a component, the preservative 1,2-benzisothiazolin-3-one at 0.035%, which contains low levels of polychlorinated dibenzodioxins and furans (TSMP Track 1). No further action is required at this time. The use of this preservative in pest control products at a maximum of 0.1% was reassessed by Health Canada in 2012 and found to be acceptable because dioxin and furan levels are low/being managed as outlined in Regulatory Directive DIR99-03 for the implementation of TSMP.

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, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Spiropidion Technical Insecticide and A20262 Insecticide, containing the active ingredient spiropidion, to control or suppress aphids, whiteflies, mealybugs, and two-spotted spider mites on terrestrial food and feed crops, and greenhouse food crops.

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
µg	microgram
°C	degrees centigrade
ºN	degree North
>	greater than
<	lesser than
≥	greater than, or equal to
≤	lesser than, or equal to
µg	microgram
A	applicator
a.i.	active ingredient
ACCase	acetyl-CoA carboxylase
ADI	acceptable daily intake
AHETF	Agricultural Handlers Exposure Task Force
AHPD	amount handled per day
AOPWIN	Atmospheric Oxidation Estimation Program for Windows
App	application
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
ATPD	area treated per day
AUC	area under the curve
BAF	bioaccumulation factor
BBCH	scale is used to identify the phenological development stages of plants
BCF	bioconcentration factor
BCF_{KLG}	growth and lipid corrected bioconcentration factor
Bq	becquerel
bw	body weight
bwg	body weight gain
CAF	composite assessment factor
Cmax	maximum plasma concentration
CAS	Chemical Abstracts Service
CCA	colony condition assessment
CEPA	*Canadian Environmental Protection Act*
cm	centimetre
cm^2	square centimetre
cm^3	cubic centimetre
CMG	common mechanism group
CO_2	carbon dioxide
CR	chemical-resistant
d	day
DAA	days after application
DA3A	days after the third application

DALA	days after last application
DEEM	Dietary Exposure Evaluation Model
DFOP	double first order in parallel
DFR	dislodgeable foliar residue
DIR	Directive
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
dw	dry weight
EC_x	effective concentration to x% of the population
ED_x	effective dose to x% of the population
EC3	concentration estimated to induce a three-fold increase in lymph node cell proliferation when compared to vehicle controls
EDE	estimated daily exposure
EEC	estimated environmental concentration
ER_x	effective rate to x% of the population
Exp	Exposure
FIR	food ingestion rate
g	gram
GD	gestation day
GHS	Globally Harmonized System of Classification and Labelling
GUS	groundwater ubiquity core
h	hour(s)
ha	hectare
HAFT	highest average field trial
HDPE	high-density polyethylene
HH	handheld
HH-MPHG	handheld mechanically pressurized handgun
HH-MPHW	handheld manually pressurized handwand
HPLC	high performance liquid chromatography
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
ICE	isolated chicken eye
ILV	independent laboratory validation
IORE	indeterminate order rate equation
IUPAC	International Union of Pure and Applied Chemistry
IRAC	Insecticide Resistance Action Committee
K_d	soil adsorption coefficient
kg	kilogram
K_{oc}	soil organic carbon-water partition coefficient
K_{ow}	octanol-water partition coefficient
kPa	kilopascal
L	litre
LAFT	lowest average field trial
LC_{50}	lethal concentration to 50% of the population
LD_{50}	lethal dose to 50% of the population
LDH	lactate dehydrogenase
LLNA	local lymph node assay
LDD_{50}	lethal dietary dose to 50% of the population
LOAEL	lowest-observed-adverse-effect level

LOC	level of concern
LOED	lowest-observed effect dose
LOQ	limit of quantitation
LR_{50}	lethal rate to 50% of the population
LSC	liquid scintillation counting
m	metre
m^2	square metre
max.	maximum
MAS	maximum average score for 24, 48 and 72 hours
mg	milligram(s)
MIS	maximum irritation score
mL	millilitre
M/L	mixer/loader
M/L/A	mixer/loader/applicator
MOA	mode of action
MOE	margin of exposure
mol	mole
MRID	US Master Record Identification Number
MRL	maximum residue limit
MRM	multiresidue method
MS	mass spectrometry
MS/MS	tandem mass spectrometry
MW	molecular weight
m/z	mass-to-charge ratio of an ion
N/A	not available
NAFTA	North American Free Trade Agreement
N/C	not calculated
N/E	not extracted
NOAEL	no-observed-adverse-effect-level
NOEC	no-observed effect concentration
NOED	no-observed effect dose
NOEDD	no-observed effect dietary dose
NOER	no-observed effect rate
NR	not reported
NZW	New Zealand White
OC	organic carbon
OECD	Organisation for Economic Co-operation and Development
OH	hydroxyl radical
OM	organic matter
PBI	plantback interval
PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
POD	point of departure
PPE	personal protective equipment
ppb	parts per billion

ppm	parts per million
PWC	Pesticide in Water Calculator
PYO	pick-your-own
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe
RA	risk assessment
RAC	raw agricultural commodity
RD	residue definition
REI	restricted entry interval
RQ	risk quotient
RTI	retreatment interval
SD	standard deviation
SFO	single first order
SOP	Standard Operating Procedure
SPN	Science Policy Note
SDEV	standard deviation
STMdR	supervised trial median residue
STMR	supervised trial mean residue
TC	transfer coefficient
TEER	transepithelial electrical resistance
TFD	terrestrial field dissipation
Tmax	time of maximum plasma concentration
TOC	total organic carbon
TP	transformation product
t_R	representative half-life
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UE	unit exposure
UF	uncertainty factor
USA	United States of America
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v	version
v/v	volume per volume
WAE	weeks after start of exposure
Yrs	Years

Appendix I Tables and figures

Table 1 Residue analysis

Matrix	Method ID	Analyte	Method type	LOQ	Reference PMRA No.
Soil	GRM069.05A	Active Metabolites: SYN547305 SYN548033 SYN549098 SYN549979	HPLC/MS-MS	1 ppb	3436607 3436608 3436613
	GRM069.13A	SYN550839 SYN548037 SYN548430			3436609 3436611 3436614
	GRM069.19A	SYN552045 SYN552257			3436610 3436612 3436615
Sediment (marine)	ECO_071_02A	Parent SYN547305		5 ppb	3436619
Ground water, surface water and seawater	GRM069.06A	Parent SYN547305		0.00005 mg/L	3436616 3436617 3436618
Fresh water	ECO_071_01E	SYN547305		1.20 mg/L	3436622
Aquatic Ecotoxicology Test Medium (Elendt M7 test medium)	ECO_071_01N	SYN548033		0.0977 mg/L	3436623
	ECO_071_01P	SYN548274		1.06 mg/L	3436624
	ECO_071_01O	SYN548430		1.0 mg/L	3436625
	ECO_071_01M	SYN549098		0.955 mg/L	3436626
	ECO_071_01L	SYN550839		0.941 mg/L	3436627
	ECO_071_01S	SYN551480		1.08 mg/L	3436628
	ECO_071_01R	SYN552045		1.07 mg/L	3436629
	ECO_071_01Q	SYN552257		1.07 mg/L	3436630
Pollen and Nectar	GRM069.03A	SYN546330 SYN547305		10 ppb	3436598 3436601 3436602

Table 2 Toxicology reference values for use in health risk assessment for spiropidion

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or target MOE
Acute dietary General population	Rat and rabbit oral developmental toxicity studies	Maternal NOAELs = 30 mg/kg bw/day Body weight loss in rats and rabbits	100
ARfD (general population) = 0.3 mg/kg bw			
Acute dietary Females 13 to 49 years old	Rat and rabbit oral developmental toxicity studies	Developmental NOAELs = 10 mg/kg bw/day Variations in the absence of maternal toxicity in rats and rabbits	300
ARfD (females 13 to 49 years old) = 0.03 mg/kg bw			
Repeated (chronic) dietary	Rat and rabbit oral developmental toxicity studies	Developmental NOAELs = 10 mg/kg bw/day Variations in the absence of maternal toxicity in rats and rabbits	300
ADI = 0.03 mg/kg bw/day			
Short- to long-term dermal[2] and inhalation[3] – adults >16 years old	Rat and rabbit oral developmental toxicity studies	Developmental NOAELs = 10 mg/kg bw/day Variations in the absence of maternal toxicity in rats and rabbits	300
Short-term dermal – children 6 to 11 years old	28-day dermal toxicity study in rats	LOAEL = 100 mg/kg bw/day Decreased cholesterol	100
Aggregate Short term oral and dermal[2] – adults >16 years old	Oral and dermal: Rat and rabbit oral developmental toxicity studies	Common endpoint: Variations in the absence of maternal toxicity in rats and rabbits Oral and dermal NOAEL = 10 mg/kg bw/day	Oral and dermal: 300
Aggregate Short term oral and dermal[2] – children 6 to 11 years old	Oral: 90-day rat oral toxicity study Dermal: 28-day rat dermal toxicity study	Common endpoint: Decreased cholesterol Oral NOAEL = 6.2 mg/kg bw/day Dermal LOAEL = 100 mg/kg bw/day	Oral and dermal: 100
Cancer	No treatment-related tumors were observed, therefore a cancer risk assessment is not required.		

[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 11% 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 Summary of new studies or revised assessments related to the toxicology of spiropidion

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Effects on organ weights are known or assumed to reflect changes in absolute weight and relative (to body weight) weight unless otherwise noted. Unless otherwise specified, studies listed in this table are considered Acceptable according to Information Note: Determining Study Acceptability for use in Pesticide Risk Assessments.

Study type/animal/PMRA No.	Study results
Toxicokinetics (inhalation – nose-only, single exposure) Rat (Wistar) PMRA No. 3436635	Acceptable with limitations Rats were administered a single dose of SYN546330 (no radiolabel) at concentrations of 0, 10, 30, 50, 80, or 200 mg/m^3 for 6 hours. Blood was collected for analysis of SYN546330 and SYN546330-enol prior to exposure and at 0.25, 0.5, 1, 2, 4, 6, 12, 24, 36, 48, 72, and 96 hours post-exposure. Levels of SYN546330 were below LOQ in most tissue samples. Tmax for SYN546330-enol typically occurred at or before the end of the 6-hour exposure. Of the animals that exhibited Tmax after the end of exposure at 12 hours, most occurred at the 10 mg/m^3 exposure level. Group mean Cmax and AUC values for each sex were all within twofold. As the exposure level increased, systemic exposure increased in a slightly less than dose proportional manner in both sexes. Limitations: limited examinations and small group sizes
Acute dermal toxicity Rat (Wistar) PMRA No. 3161306	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity were observed. Low acute dermal toxicity
Acute inhalation toxicity (nose-only) Rat (Wistar) PMRA No. 3161307	LC_{50} > 1.12 mg/L (♂/♀) Clinical signs of toxicity included, ↓ activity, noisy and laboured respiration, incoordination, clonic convulsion, prone position, cold to the touch. Slight acute inhalation toxicity

Study type/animal/PMRA No.	Study results
Skin irritation Rabbit (NZW) PMRA No. 3161308	MAS = 0 MIS = 0 Non-irritating
Eye irritation Rabbit (NZW) PMRA No. 3161309	MAS = 0 MIS = 4.7 at 1 hour Non-irritating
In vitro eye irritation Isolated chicken eyes PMRA No. 3161310	Acceptable with limitations Corneal swelling was not observed in any of the eyes. Slight corneal opacity and slight fluorescein retention was observed in all three eyes throughout the observation period. The test item adhered to the cornea surfaces and was unable to be cleared after 240 minutes. Thus, the test item could not be classified as a non-irritant or a severe irritant. Limitations: study design and results precluded classification for eye irritation potential.
Skin sensitization (LLNA) Mice (CBA/Ca) PMRA No. 3161311	Positive EC3 = 0.13% Potential dermal sensitizer
1-year oral (capsule) Dog (Beagle) PMRA No. 3161321	NOAEL = 10 mg/kg bw/day (♂/♀) LOAEL = 30 mg/kg bw/day (♂/♀) Effects at LOAEL: mortality (1/sex); ♂ sacrificed in extremis on Day 14 and clinical signs included incoordination, salivation and lying on side; ♀ sacrificed on Day 7 and clinical signs included tremors, subdued behaviour, decreased activity, lying on side and hypersensitivity (note that dosing at 30 mg/kg bw/day was stopped on Day 15 due to adverse clinical observations and mortalities).
28-day dermal Rat (Wistar) PMRA No. 3161322	NOAEL = not established/100 mg/kg bw/day (♂/♀) LOAEL = 100/300 mg/kg bw/day (♂/♀) Effects at LOAEL: ↓ cholesterol (♂/♀); ↓ bwg (♀)

Study type/animal/PMRA No.	Study results
In vitro airway irritation Mucilair™ Airway Model Model of human airway epithelium derived from human airway cells PMRA No. 3436634	Acceptable with limitations ≥ 126 mg/L: necrotic cells in respiratory epithelium 317 mg/L: minor thinning of epithelium No change in TEER or LDH release or in resazurin metabolism. No evidence of cytotoxicity, altered cell membrane integrity, diminished monolayer integrity, or altered cell viability at any concentration tested. Limitations: limited reporting, exposed cells representative of a single region of the respiratory tract, lack of analytic verification of the amount of active agent present in the model system during or after exposures, limited information related to donor pool.
Short-term repeated inhalation – 5-day tolerability study (nose-only) Rat (Sprague Dawley) PMRA No. 3436633	Acceptable with limitations ≥ 0.099 mg/L (equivalent to approximately 26 mg/kg bw/day): ↓ bw, ↓ bwg (♂/♀) ≥ 0.220 mg/L (equivalent to approximately 57 mg/kg bw/day): mortality (4 ♂, 1 ♀ at this dose level), dirty hair, soiled and moisture in perineum (♂/♀) 0.537 mg/L (equivalent to approximately 140 mg/kg bw/day): ↓ activity (♂/♀); mortality (3 ♂) Gross pathology findings in animals found dead included stomach and cecum distention with gas. Microscopic pathology in animals found dead included various degrees of pulmonary diffuse congestion with hemorrhage and various degrees of pulmonary edema. This study was conducted as a preliminary dose range-finding study for the potential conduct of a 28-day inhalation toxicity study in rats. Based on these results, the study investigators suggested that dose levels of 0, 0.030, 0.050, and 0.080 mg/L be used in the main study as these dose levels are expected to be tolerable for rats. Limitations: non-guideline exploratory study with small group sizes.

Study type/animal/PMRA No.	Study results
Repeat-exposure inhalation toxicity – Waiver Request PMRA No. 3436632	Both spiropidion and the associated end-use product A20262 Insecticide are of low acute inhalation toxicity. In the 5-day inhalation toxicity tolerability study in rats, the maximum tolerated dose was estimated to be 0.099 mg/L (equivalent to approximately 26 mg/kg bw/day). Using the MucilAir^{TM} airway model, spiropidion did not induce chemical-mediated irritation at concentrations below 126 mg/L. Histopathological effects were observed at the highest concentrations as evidenced by thinning of the membrane and necrosis of respiratory epithelium. However, the TEER, LDH, and resazurin assays did not show evidence of toxicity at any concentration of spiropidion tested. Based on the results of the acute inhalation and 5-day inhalation toxicity tolerability studies, lung-related macroscopic effects occur only at concentrations of spiropidion that cause mortality-induced lung-related macroscopic effects. At non-lethal doses, spiropidion exposure results in transient inhalation-related clinical signs of toxicity as well as body weight changes indicating there may be route-specific toxicity via the inhalation route. The lowest exposure concentration recommended for the conduct of a subchronic inhalation toxicity study in rats was 0.030 mg/L, equivalent to an internal exposure level of approximately 7.8 mg/kg bw/day. However, a standard repeat-exposure inhalation toxicity study does not assess developmental toxicity endpoints including skeletal variations, which are the endpoints of concern in the spiropidion database. The developmental NOAEL established by Health Canada of 10 mg/kg bw/day would be equivalent to an external inhalation exposure concentration of approximately 0.04 mg/L/day. Based on a weight-of-evidence assessment of the information presented above, a repeat-dose exposure inhalation toxicity study in rodents is unlikely to provide information critical to assessing potential risks from inhalation exposure to spiropidion.
Developmental toxicity (gavage) Rabbit (NZW) PMRA No. 3161346, 3161350	Maternal NOAEL = 30 mg/kg bw/day Maternal LOAEL = 60 mg/kg bw/day Effects at LOAEL: bw loss (GD 6-12) Developmental NOAEL = 10 mg/kg bw/day Developmental LOAEL = 30 mg/kg bw/day Effects at LOAEL: ↑ incidence of incomplete 2nd cartilaginous dorsal plate of the cervical vertebrae and incomplete xiphoid cartilage of the sternum. No treatment-related malformations Evidence of sensitivity of the young

Study type/animal/PMRA No.	Study results
Bacterial reverse mutation assay Metabolite SYN549098 S. typhimurium TA100, TA98, TA1535, TA1537; E coli WP2 (pKM101), WP2 uvrA (pKM101) PMRA No. 3436636	Negative ± metabolic activation Tested up to a limit concentration
In vitro mammalian cell assay Metabolite SYN549098 Hamster V79 cells PMRA No. 3436638	Negative ± metabolic activation Tested up to the limit of solubility
In vitro micronucleus assay Metabolite SYN549098 Human lymphocytes PMRA No. 3436637	Negative ± metabolic activation Tested up to the limit of solubility

Table 4 Acute toxicity profile of A20262 insecticide containing spiropidion

Study type/animal/PMRA No.	Study results
Acute oral toxicity (Up and Down) Rat (Wistar) PMRA No. 3161389	LD_{50} > 5000 mg/kg bw (♀) Clinical signs of toxicity included irritability, incoordination, piloerection, hunched back, ↓ activity, tonic convulsion, prone position, vocalization and ↑ salivation. Clinical signs resolved by Day 9. Low acute oral toxicity

Study type/animal/PMRA No.	Study results
Acute dermal toxicity Rat (Wistar) PMRA No. 3436476	LD_{50} > 5000 mg/kg bw (♂/♀) No clinical signs of toxicity were observed. Low acute dermal toxicity
Acute inhalation toxicity (nose-only) Rat (Wistar) PMRA No. 3436477	LC_{50} > 2.75 mg/L (♂/♀) Clinical signs of toxicity included labored, noisy and gasping respiration and lack of grooming. Clinical signs resolved by Day 4. Low acute inhalation toxicity
Eye irritation Rabbits (NZW) PMRA No. 3436480	MAS = 0 MIS = 4 (at 1 h) Non-irritating to the eye
In vitro eye irritation (OECD 438) Isolated chicken eyes PMRA No. 3436481	No corneal swelling or fluorescein retention (ICE Class I), but slight corneal opacity (ICE Class II), observed. Overall ICE Class 2xI 1XII (GHS No category). Non-irritating to the eye
Dermal irritation Rabbits (NZW) PMRA No. 3436479	MAS = 0 MIS = 0 Non-irritating to the skin
In vitro dermal irritation (OECD 439) Reconstructed human epidermis PMRA No. 3436478	Mean cell viability of 92.8% (GHS No Category) Non-irritating to the skin
Dermal sensitization (LLNA) CBA/J mice PMRA No. 3436482	Positive EC3 = 0.76% Potential dermal sensitizer

3000 µg/cm^2 = Formulation Concentrate; 20 µg/cm^2 = High Spray Dilution 1; 8 µg/cm^2 = Medium Spray Dilution; 2 µg/cm^2 = Low Spray Dilution. SD = Standard deviation. Cells highlighted in gray are calculations performed by Health Canada using raw data from the study review.

[1] Total non-absorbed = sum of 8h and 24h non-absorbed doses.

[2] Total *stratum corneum* (tape strips) is the sum of all tape strips 1-20.

[3] Total skin is the sum of the tape strips, unexposed skin and application skin site.

[4] Recovery is the sum of the total non-absorbed dose + total skin + receptor fluid (including chamber wash).

[5] Dermal absorption is based on the sum of skin (application skin site, unexposed skin and tape strips) + receptor fluid (including chamber wash).

Table 5 Summary of human in vitro dermal absorption study results

	Percent applied dose (%)							
	3000 µg/cm²		20 µg/cm²		8 µg/cm²		2 µg/cm²	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Skin Wash 8 h	38.66	11.49	27.66	18.36	49.76	22.22	42.23	16.94
Tissue Swab 8 h	57.19	15.95	70.75	18.15	45.90	27.03	31.08	15.61
Pipette Tip 8 h	0.05	0.07	0.05	0.08	0.10	0.15	0.10	0.16
Total Non-absorbed Dose 8 h	95.90	5.59	98.45	1.96	95.76	8.05	73.40	20.19
Skin Wash 24 h	2.57	3.07	0.66	0.39	2.05	1.20	5.97	1.90
Tissue Swab 24 h	1.20	1.56	0.51	0.45	1.17	0.82	3.50	1.97
Pipette Tip 24 h	0.00	0.01	0.00	0.00	0.01	0.01	0.02	0.02
Donor Chamber Wash	1.03	0.70	0.14	0.14	0.22	0.14	0.54	0.42
Total Non-absorbed Dose 24 h	4.80	4.96	1.31	0.84	3.44	2.03	10.03	3.69
Total Non-absorbed Dose[1]	100.70	1.06	99.77	1.81	99.20	7.36	83.44	20.37
Total *Stratum corneum* (Tape Strips)[2]	0.45	0.18	0.53	0.02	1.22	0.03	3.51	0.24
Unexposed Skin	0.00	0.01	0.00	0.00	0.01	0.03	0.03	0.04
Application Skin Site	0.09	0.08	0.89	0.67	2.61	1.50	5.86	2.27
Total Skin[3]	**0.54**	**0.09**	**1.42**	**0.38**	**3.84**	**0.85**	**9.40**	**1.24**
Receptor Fluid	0.02	0.01	0.14	0.11	0.33	0.24	1.08	0.68
Receptor Chamber Wash	0.01	0.01	0.01	0.01	0.01	0.01	0.04	0.03
Recovery[4]	101.37	1.15	101.3	1.68	103.4	7.09	93.95	20.16
Dermal Absorption[5]	**0.62**	**0.54**	**1.56**	**0.73**	**4.18**	**1.81**	**10.51**	**1.66**

3000 µg/cm² = Formulation Concentrate; 20 µg/cm² = High Spray Dilution 1; 8 µg/cm² = Medium Spray Dilution; 2 µg/cm² = Low Spray Dilution. SD = Standard deviation. Bolded cells are calculations performed by Health Canada using raw data from the study review.

[1] Total non-absorbed = sum of 8h and 24h non-absorbed doses.

[2] Total *stratum corneum* (tape strips) is the sum of all tape strips 1-20.

[3] Total skin is the sum of the tape strips, unexposed skin and application skin site.

[4] Recovery is the sum of the total non-absorbed dose + total skin + receptor fluid (including chamber wash).

[5] Dermal absorption is based on the sum of skin (application skin site, unexposed skin and tape strips) + receptor fluid (including chamber wash).

Table 6 Unit Exposure (UE) value estimates for mixers, loaders and applicators (µg/kg a.i. handled)

Exposure scenario and PPE	Dermal (µg/kg a.i. handled)	Inhalation[1] (µg/kg a.i. handled)
PPE: Single layer and chemical-resistant (CR) gloves		
Mixer/loader		
Liquid/open mix/load (AHETF)	58.50	0.63
Applicator		

Exposure scenario and PPE	Dermal (µg/kg a.i. handled)	Inhalation[1] (µg/kg a.i. handled)
Liquid/open cab groundboom application (AHETF)	25.4	1.68
Liquid/open cab airblast application without a CR hat (AHETF)	3769.3	9.08
Mixer/loader/applicator (PHED)		
Liquid/open pour/backpack	5445.85	62.1
Liquid/open pour/mechanically pressurized handguns	5585.49	151
Liquid/open pour/manually pressurized handwands	943.37	45.20
Mixer/loader/applicator (AHETF)		
Liquid/open mix/load + liquid/open cab groundboom	83.90	2.31
Liquid/open mix/load + liquid/open cab airblast application without a CR hat	3827.80	9.71

[1] Light inhalation rate except for backpack which is moderate.

Table 7 Occupational mixer/loader/applicator exposure and risk assessment

Application method	Rate[1]	ATPD/AHPD[2]	Exposure[3] (µg/kg bw/day)		MOE[4]		
			Dermal	Inhalation	Dermal	Inhalation	Combined
Single layer, CR Gloves (MLA)							
Leafy Vegetables, Brassica Head and Stem Vegetables, Fruiting Vegetables, Cucurbit Vegetables							
Groundboom	0.18 kg a.i./ha	26 ha	0.54	0.14	18500	74 000	14 800
Pome Fruits, Grapes							
Airblast	0.2 kg a.i./ha	20 ha	21.1	0.49	475	20 600	464
Pome Fruits							
HH-Backpack	0.50 g a.i./L	150 L	0.56	0.058	17800	172 000	16 100
HH-MPHG	0.50 g a.i./L	3800 L	14.6	3.59	685	2700	550
HH-MPHW	0.50 g a.i./L	150 L	0.10	0.04	102000	236 000	71 600
Grapes							
HH-Backpack	0.40 g a.i./L	150 L	0.45	0.05	22 300	215 000	20 200
HH-MPHG	0.40 g a.i./L	3800 L	11.7	2.87	857	3490	688
HH-MPHW	0.40 g a.i./L	150 L	0.08	0.03	128 000	295 000	89 500

Application method	Rate[1]	ATPD/AHPD[2]	Exposure[3] (µg/kg bw/day)		MOE[4]		
			Dermal	Inhalation	Dermal	Inhalation	Combined
Greenhouse vegetables							
HH-Backpack	0.48 g a.i./L	150	0.54	0.06	18 500	179 000	16 800
HH-MPHG	0.48 g a.i./L	3800	14.0	3.44	714	2900	573
HH-MPHW	0.48 g a.i./L	150	0.09	0.04	107 000	246 000	74 600

ATPD = Area Treated Per Day, AHPD = Amount Handled Per Day, MOE = Margin of Exposure, CR = Chemical Resistant, HH-MPHG = Handheld Mechanically Pressurized Handgun, HH-MPHW = Handheld Manually Pressurized Handwand

[1] Rate for handheld equipment based on the maximum rate per application divided by the lowest spray volume

[2] Standard Area Treated/Amount Handled per Day values

[3] Exposure = (Unit exposure × ATPD × Rate × Absorption (11% dermal and 100% inhalation)) / (80 kg bw)

[4] Based on NOAEL = 10 mg/kg bw/day; Target MOE = 300

Table 8 Postapplication exposure and risk estimates to workers for spiropidion on Day 0 after the Last Application

Crop group	Activity	TC (cm^2/h)[1]	Rate (kg/ha)	No. Apps / Season	RTI (days)	Peak DFR[2]	Exposure estimates		REI (days)[5]
							Exp[3]	MOE[4]	
Crop Group 4-13 Leafy Vegetables	Hand Weeding	4400	0.18	3	7	0.77	37.2	**270**	1
	Irrigation (hand set)	1750					14.8	680	0.5
Crop Group 5-13 Brassica Head and Stem Vegetables	Hand Harvesting	5150	0.18	3	7	0.77	43.5	**230**	3
	Hand Weeding	4400					37.18	**270**	1
	Scouting (Full)	4000					33.80	300	0.5
Crop Group 8-09 Fruiting Vegetables; Crop Group 9 Cucurbit Vegetables	Irrigation (hand set)	1750	0.18	3	7	0.77	14.8	680	0.5
Crop Group 11-09 Pome Fruits	Hand Thinning	3000	0.2	3	7	0.85	28.2	355	0.5
Grapes	Girdling, Turning	19300	0.2	3	7	0.85	181	**55**	16
	Hand Harvesting, Hand Leaf Pulling, Tying / Training	8500					79.8	**125**	8

Crop group	Activity	TC (cm^2/h)[1]	Rate (kg/ha)	No. Apps / Season	RTI (days)	Peak DFR[2]	Exposure estimates		REI (days)[5]
							Exp[3]	MOE[4]	
	Irrigation (hand set)	1750					16.4	610	0.5
Greenhouse vegetables	All Activities	1400	0.144	2	7	0.67	10.4	970	0.5

Activities with risks of concern are **bolded**

TC = Transfer Coefficient, No. Apps/Season = Number of Applications per Season/Crop Cycle, RTI = Retreatment Interval, Peak DFR = Dislogeable Foliar Residue as Percent of the application Rate (µg/cm^2), Exp = Exposure (µg/kg bw/day), MOE = Margin of Exposure, REI = Restricted-Entry Interval

1 Standard Transfer Coefficients.

2 Calculated using the standard 25% dislodgeable on the day of application and 10% dissipation per day for outdoor scenario and 2% for greenhouse crops.

3 Exposure (µg/kg bw/day) = (Peak DFR [µg/cm^2] × TC [cm^2/h] × 8 hours × 11% dermal absorption]) / (80 kg bw)

4 Based on a NOAEL of 10 mg/kg bw/day, Target MOE = 300

5 Minimum REI is 12 hours (or 0.5 days) to allow residues to dry, suspended particles to settle and vapours to dissipate.

Table 9 Postapplication dermal exposure and risk estimates to residents on Day 0 from pome fruit trees treated commercially with spiropidion

Crop (Max Rate; No. App/season)	Life stage	Peak DFR (µg/cm^2)[1]	TC (cm^2/h)[2]	Exposure duration (h/day)	Dermal exposure (mg/kg bw/day)[3]	MOE[4]	REI
Pome fruits (0.2 kg a.i./ha; 3)	Adults (16+ yrs)	0.85	1700	1	2.0×10^{-3}	5000	Until sprays have dried
	Children (6 < 11 yrs)		930	0.5	1.24×10^{-2}	8060	

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

1 Calculated using the standard value of 25% of the application rate on Day 0 after the last application and 10% dissipation per day. The DFR value was calculated based on 3 applications at the highest rate for pome trees and a RTI of 7 days.

2 A single TC is representative of all activities in residential fruit trees. TCs were obtained from 2012 USEPA SOP for Residential Pesticide Exposure Assessment.

3 Dermal Exposure = (Peak DFR [µg/cm^2] × TC [cm^2/h] × Exposure duration [h/day] × [11% dermal absorption]) / (Body weight [80 kg for adults; 32 kg for children] × 1000 µg/mg).

4 Adult MOE based on a NOAEL of 10 mg/kg bw/day with a target MOE of 300; Children MOE based on a LOAEL of 100 mg/kg bw/day with a target MOE of 100.

Table 10 Aggregate exposure and risk estimates for spiropidion

Life Stage	Exposure (mg/kg bw/day)			MOE
	Dermal[1]	Dietary[2]	Aggregate[3]	
Adult (16+ yrs) [1]	2.0×10^{-3}	2.09×10^{-3}	4.08×10^{-3}	2450 [4]
Children (6 to < 11 yrs) [2]	1.24×10^{-2}	2.88×10^{-3}	-	1700 [5]

MOE = Margin of Exposure

1 Refer to Postapplication Dermal Exposure and Risk Estimates Table (Table 9)

2 Refer to the Chronic Dietary Exposure Table (Table 15)

[3] Aggregate Exposure (adult) = Dermal Exposure + Dietary Exposure. An aggregate exposure value was not calculated for children due to the different oral and dermal toxicological reference values for the common aggregate endpoint

[4] Aggregate MOE (adult) = NOAEL of 10 mg/kg bw/day ÷ Aggregate Exposure; Target MOE = 300.

[5] Aggregate MOE (children) =

[Phényl-U-^{14}C]-spiropidion		
Pasteurisation	**Cuisson, brassage et ébullition**	**Stérilisation**
pH 4/90 °C/20 min	**pH 5/100 °C/60 min**	**pH 6/120 °C/20 min**

1/(((1/(Dermal LOAEL of 100 mg/kg bw/day /Dermal Exposure)) + ((1/(Oral NOAEL of 6.2 mg/kg bw/day/Dietary Exposure))); Target MOE = 100.

Table 11 Summary of most recent dietary exposure assessments (DEAs) of the tetronic and tetramic acid derivatives, with risk estimates adjusted to reflect the human health reference value (HHRV) based on the common effect of this cumulative assessment group (CAG)

Active ingredient	**Spiropidion**		**Spirodiclofen**		**Spiromesifen**		**Spirotetramat**	
Year of most recent DEA	Current assessment (proposed use)		2011		2023		2017	
ADI used in DEA (mg/kg bw/day)	0.03		0.014		0.007		0.02	
x-fold difference between HHRV of common effect and ADI	1.9× higher		5.6× higher		2.9× higher		3.8× higher	
Subpopulation	**Chronic dietary risk estimates (food + drinking water) (% ADI)**							
	Existing	Adjusted	Existing	Adjusted	Existing	Adjusted	Existing	Adjusted
General population	7.8	4.1	1.4	0.25	31.3	10.8	9.3	2.4
All Infants	12.8	6.7	4.6	0.82	54.5	18.8	18.3	4.8
Children 1-2 years	20.2	10.6	2.4	0.43	56.1	19.3	26.2	6.9
Children 3-5 years	14.8	7.8	2.2	0.39	45.4	15.7	19.9	5.2
Children 6-12 years	8.6	4.5	1.4	0.25	30.6	10.6	11.5	3.0
Youth 13-19 years	5.2	2.7	1.0	0.18	23.1	8.0	7.1	1.9
Adults 20-49 years	6.8	3.6	1.3	0.23	29.7	10.2	7.3	1.9
Adults 50+ years	7.5	3.9	1.4	0.25	31.1	10.7	8.2	2.2

Active ingredient	Spiropidion		Spirodiclofen		Spiromesifen		Spirotetramat	
Females 13-49 years	N/C	N/C	1.3	0.23	30.3	10.4	7.2	1.9

N/C = not calculated, for this subpopulation as there is no ADI established specifically for females 13-49, and thus risk for this subpopulation is covered by the risk estimates for adults and youth.
Existing risk estimates are from the dietary exposure assessments (DEAs) of the individual active ingredient
Adjusted risk estimate (% ADI) = Existing risk estimate (% ADI) / (x-fold difference between HHRV of common effect and ADI)

Table 12 Cumulative dietary risk assessment of tetronic and tetramic acid derivatives

Subpopulation	Adjusted chronic dietary risk estimates (food + drinking water)				Cumulative dietary risk (% risk cup)
	Spiropidion (% ADI)	Spirodiclofen (% ADI)	Spiromesifen (% ADI)	Spirotetramat (% ADI)	
General population	4.1	0.25	10.8	2.4	17.6
All Infants	6.7	0.82	18.8	4.8	31.2
Children 1-2 years old	10.6	0.43	19.3	6.9	37.3
Children 3-5 years old	7.8	0.39	15.7	5.2	29.1
Children 6-12 years old	4.5	0.25	10.6	3.0	18.4
Youth 13-19 years old	2.7	0.18	8.0	1.9	12.7
Adults 20-49 years old	3.6	0.23	10.2	1.9	16.0
Adults 50+ years old	3.9	0.25	10.7	2.2	17.1
Females 13-49 years old	N/C	0.23	10.4	1.9	N/C

N/C = not calculated, as for this subpopulation as there is no ADI established specifically for females 13-49, and thus risk for this subpopulation is covered by the risk estimates for adults and youth.

Table 13 Residue analysis in plant matrices

Analytical methods	Matrices	Analytes	Method ID/type	LOQ	Reference (PMRA No.)
Plant commodities					
Enforcement Method	Zucchini fruit, soybean seed, dry broad bean, potato tuber, orange whole fruit	Spiropidion and metabolites SYN547305, SYN547435, SYN548430	QuEChERS BPL19-0035/ LC-MS/MS	0.01 ppm/analyte	3161293
ILV of Enforcement Method	Zucchini fruit, dry bean		QuEChERS BPL19-0035/ LC-MS/MS	0.01 ppm/analyte	3161289
Radiovalidation	Cotton (seed, trash, foliage), potato (tubers), tomato fruit		QuEChERS BPL19-0035/ LC-MS/MS	0.01 ppm/analyte	3436646

Analytical methods	Matrices	Analytes	Method ID/type	LOQ	Reference (PMRA No.)
Data-Gathering Method	Apple fruit, zucchini fruit, tomato fruit, citrus fruit, potato tuber, wheat grain, dry beans, soybean seed, hay	Spiropidion and metabolites SYN547305, SYN547435, SYN548430	GRM069.04A/ LC-MS/MS	0.01 ppm/analyte	3161285, 3161287
	Apple, tomato, soybean, bean, wheat grain, potato, orange, wheat straw	Spiropidion and metabolite SYN547305	GRM069.02A/ LC-MS/MS	0.01 ppm/analyte	3161288, 3161290
	Radish tops, radish roots, wheat grain, wheat straw, carrots, spinach	Spiropidion and metabolites SYN547305, SYN548430, SYN550821, SYN549937, SYN548033, SYN550838	GRM069.08A/LC-MS/MS	0.01 ppm/analyte	3436605, 3436596
	Radish leaves, radish roots, wheat grain, wheat straw, carrots, spinach	SYN549098	GRM069.10A/LC-MS/MS	0.01 ppm/analyte	3436599, 3436606
	Corn oil	Spiropidion and metabolites SYN547305, SYN547435, SYN548430, SYN550820, SYN550839	GRM069.12A/LC-MS/MS	0.01 ppm/analyte	3436604
		Spiropidion and metabolites SYN547305, SYN547435, SYN548430			3436600

Table 14 Integrated food residue chemistry summary

Nature of the residue in tomato	**PMRA No. 3161365**
Radiolabel position	[phenyl-U-14C] (specific activity: 2.48 MBq/mg); [spiro-5-14C] (specific activity: 2.35-2.38 MBq/mg)
Treatment	

Nature of the residue in tomato		PMRA No. 3161365
Test site	In individual pots in greenhouse	
Treatment	Three foliar applications at BBCH 16, 61, and 85	
Total rate	[phenyl-U-14C]-label: 3 × 283.3-293.4 g a.i./ha; Total rate of 862.4 g a.i./ha; [spiro-5-14C]-label: 3 × 272.8-301.9 g a.i./ha; Total rate of 861.0 g a.i./ha	
Formulation	Suspension concentrate formulation of spiropidion	
Harvest	Immature fruit and foliage were harvested at PHIs of 31 days after application 2 (31DAA2), and mature fruit and foliage were harvested at PHIs of 1 and 21 days after application 3 (1DAA3 and 21DAA3). Samples of immature fruit and foliage (31DAA2) and mature foliage (1DAA3) were collected but not analyzed.	
Extraction solvents	Mature Tomato Fruit (1DAA3 and 21DAA3): Surface wash (immersed three times in acetonitrile) + solvent extraction (2 × acetonitrile:water (8:2) + 1 × acetonitrile:water (1:1)). Mature Tomato Foliage (21DAA3): Solvent extraction (2 x acetonitrile:water (8:2) + 1 × acetonitrile:water (1:1)). PES: Residues in PES were low and therefore not analyzed further.	
Matrices	**PHI (days)**	**[phenyl-U-14C]/[spiro-5-14C] TRR (ppm)**
Mature tomato fruit	1	0.117–0.153
Mature tomato fruit	21	0.073–0.174
Mature tomato foliage	21	0.502–2.480
Summary of major metabolites in tomatoes		
Matrices	[phenyl-U-14C]/[spiro-5-14C]	
Mature tomato fruit	Spiropidion, SYN548430	
Mature tomato fruit	Spiropidion, SYN547305, SYN548430	
Mature tomato foliage	Spiropidion, SYN547305, SYN548430	

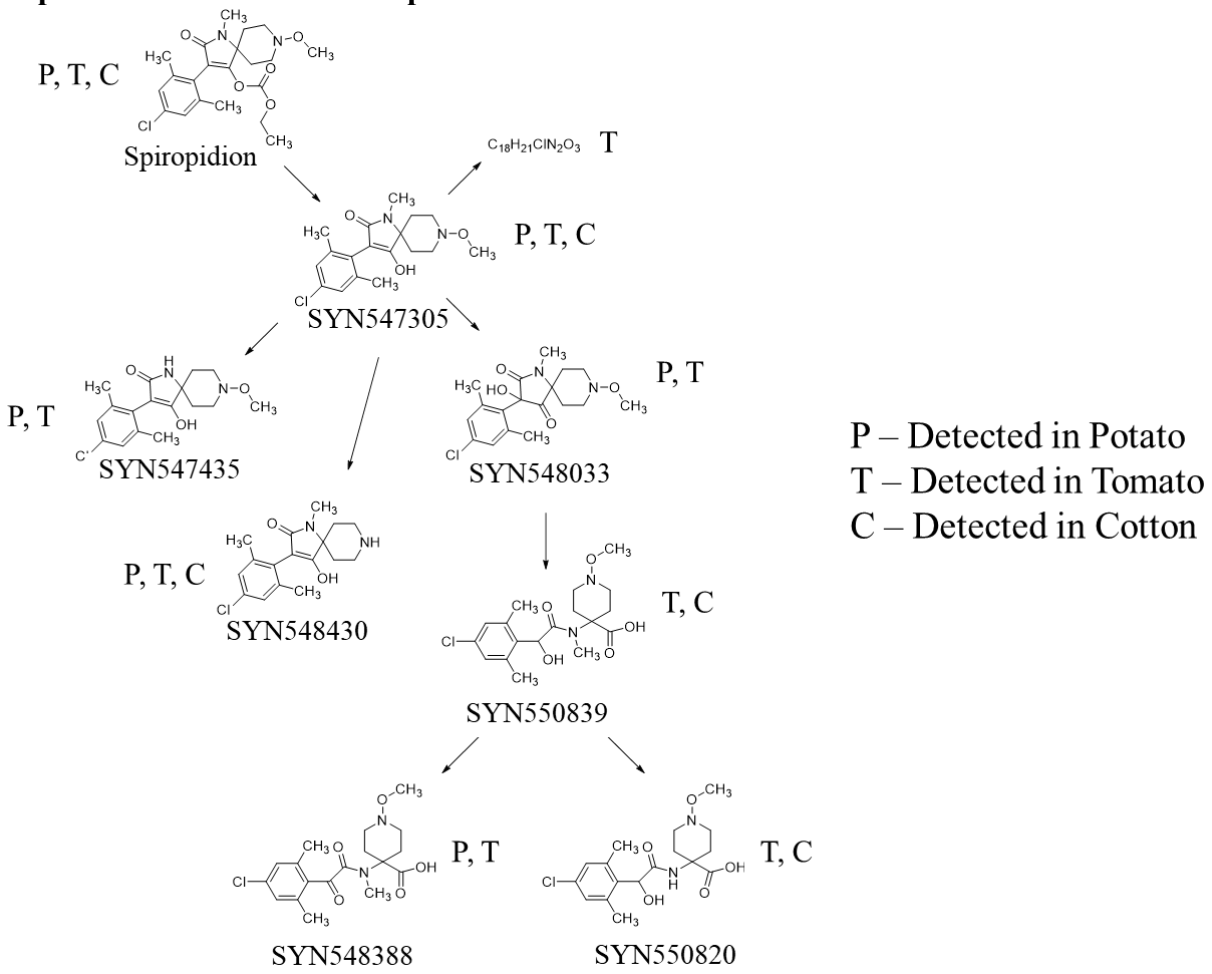
Nature of the residue in cotton		PMRA No. 3161366
Radiolabel position	[phenyl-U-14C] (specific activity: 2.48 MBq/mg); [spiro-5-14C] (specific activity: 2.35 MBq/mg)	
Treatment		
Test site	In individual pots in greenhouse	
Treatment	Three foliar applications at BBCH 16, 60, and 87	
Total rate	[phenyl-U-14C]-label: 3 × 148.8-154.8 g a.i./ha; Total rate of 453.6 g a.i./ha; [spiro-5-14C] -label: 3 × 150.3-156.0 g a.i./ha; Total rate of 459.9 g a.i./ha	
Formulation	Suspension concentrate formulation of spiropidion	
Harvest	Immature foliage: 27 days after application 2 Mature seeds, fibre (gin), and trash (burrs, leaves, stems, and immature seeds): 14 days after application 3 Samples of cotton fibre (gin) were collected but not analyzed.	

Nature of the residue in cotton		PMRA No. 3161366
Extraction solvents	Immature foliage and mature trash: Solvent extraction (2 × acetonitrile:water (8:2, v/v) + 1 × acetonitrile:water (1:1, v/v)). Mature seed: Solvent extraction (2 × acetonitrile:water (8:2, v/v), 1 × hexane, 1 × acetonitrile:water (1:1, v/v)). PES: PES from immature foliage was sequentially extracted with acetone, protease, driselase, mineral base (NaOH), and mineral acid (HCl). PES from mature seed was extracted with protease. PES of mature trash was not subjected to additional extraction procedures.	
Matrices	**PHI (days)**	**[phenyl-U-14C]/[spiro-5-14C] TRR (ppm)**
Immature foliage	27	0.537–1.743
Mature seeds	14	0.029–0.034
Mature trash	14	2.674–3.431
Summary of major metabolites in cotton		
Matrices	[phenyl-U-14C]/[spiro-5-14C]	
Immature foliage	Spiropidion, SYN550820	
Mature seeds	SYN547305	
Mature trash	Spiropidion, SYN547305, SYN550820, SYN550839	

Nature of the residue in potato		PMRA No. 3161367
Radiolabel position	[phenyl-U-14C] (specific activity: 2.48 MBq/mg); [spiro-5-14C] (specific activity: 2.35-2.38 MBq/mg)	
Treatment		
Test site	In individual pots in greenhouse	
Treatment	Three foliar applications at BBCH 16, 42, and 48	
Total rate	[phenyl-U-14C]-label: 3 × 193.3-197.1 g a.i./ha; Total rate of 585.9 g a.i./ha; [spiro-5-14C]-label: 3 × 192.1-199.7 g a.i./ha; Total rate of 590.2 g a.i./ha	
Formulation	Suspension concentrate formulation of spiropidion	
Harvest	Immature potato tubers and foliage were harvested 23 days after application 2. Mature potato tubers and foliage were harvested 7 days after application 3.	
Extraction solvents	Homogenized samples: 2 × acetonitrile:water (8:2, v/v) and 1 × acetonitrile:water (1:1). PES: Due to low TRRs in PES, they were not extracted further.	
Matrices	PHI (days)	[phenyl-U-14C]/[spiro-5-14C] TRR (ppm)
Immature foliage	23	2.863–2.938
Immature tubers	23	0.032–0.033
Mature foliage	7	13.269–23.092

Nature of the residue in potato		PMRA No. 3161367
Mature tubers	7	0.061–0.074
Summary of major metabolites in potatoes		
Matrices	[phenyl-U-14C]/[spiro-5-14C]	
Immature foliage	Spiropidion	
Immature tubers	SYN547305, SYN547435	
Mature foliage	Spiropidion, SYN547305	
Mature tubers	SYN547305, SYN547435	

Proposed metabolic scheme in plants



Freezer storage stability in plant matrices			PMRA No. 3161357, 3161358, 3161359, 3161363, 3161364, 3436643 (primary crops); 3161355, 3436641 (processed crops); 3436644 (secondary crops)	
Tested matrices	**Analytes**	**Tested intervals (months)**	**Temperature (°C)**	**Category**
Primary crops				
Apple fruit	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	High-water
Dried bean	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	High-protein
Potato tuber	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	High-starch
Wheat grain		0, 1, 7.4, 10, 12, 18, 24		
Barley grain		0, 1, 2, 3, 6, 9, 18, 24		
Soybean seed	Spiropidion, SYN547305	0, 0.5, 1, 2, 3, 6, 9, 12, 15, 21, 24	≤ -18	High-oil
Cotton seed		0, 1, 3, 6, 9, 12, 20, 24		
Orange fruit	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	High-acid
Wheat straw	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	Misc. crop
Processed commodities				
Dried tomato	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18	≤ -18	High-water
Tomato paste		0, 1, 3, 6, 9, 12, 18		
Corn meal	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18	≤ -18	High-starch
Potato flakes		0, 1, 3, 6, 9, 12, 18		
Corn oil	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18	≤ -18	High-oil
Soybean meal		0, 1, 3, 6, 9, 12, 18		
Orange juice	Spiropidion, SYN547305	0, 1, 3, 6, 9, 12, 18	≤ -18	High-acid
Secondary crops				
Radish leaves	Spiropidion, SYN549098	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	High-water
Spinach		0, 1, 3, 6, 9, 12, 18, 24		

Freezer storage stability in plant matrices			PMRA No. 3161357, 3161358, 3161359, 3161363, 3161364, 3436643 (primary crops); 3161355, 3436641 (processed crops); 3436644 (secondary crops)	
Radish roots	Spiropidion, SYN549098	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	High-starch
Wheat grain		0, 1, 3, 6, 9, 12, 18, 24		
Carrot		0, 1, 3, 6, 9, 12, 18, 24		
Wheat straw	Spiropidion, SYN549098	0, 1, 3, 6, 9, 12, 18, 24	≤ -18	Misc. crop

Crop field trials and residue decline	PMRA No. 3161375, 3161379, 3436654, 3436651, 3161377, 3436656, 3436655, 3161378, 3436653, 3436647, 3436652, 3436650, 3436648, 3436649, 3161376

Spiropidion (A20262B; containing 300 g a.i./L; SC) was applied to various crops during the 2017-2021 growing seasons. Spiropidion was applied as a foliar treatment in accordance with the approved use directions. An adjuvant was added to the spray mixture for all applications. Residue decline data show that residues of spiropidion and SYN547305 generally decreased with increasing preharvest intervals (PHIs). The number and geographic distribution of the submitted trials were generally in accordance with Health Canada's DIR2010-05 or SPN2017-02. 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)	Analyte	Residue levels (ppm)[1]					
				n	LAFT	HAFT	Median	Mean	SDEV
Potato tuber	343-373	6-22	Spiropidion	26	<0.01	<0.01	<0.01	<0.01	0.000
			SYN547305		<0.01	0.886	0.228	0.327	0.279
			Combined[2]		0.02	0.896	0.238	0.337	0.279
Leaf lettuce	527-548	1-3	Spiropidion	8	0.025	2.850	0.897	1.006	0.952
			SYN547305		0.102	1.306	0.699	0.689	0.410
			Combined[2]		0.127	3.715	1.748	1.694	1.150
Head lettuce (With Wrapper Leaves)	536-549	1	Spiropidion	8	0.021	0.926	0.454	0.478	0.344
			SYN547305		0.070	0.979	0.509	0.515	0.346
			Combined[2]		0.090	1.759	1.068	0.994	0.665
Spinach	534-549	1-9	Spiropidion	9	0.029	0.786	0.300	0.330	0.240
			SYN547305		1.362	9.595	3.370	3.834	2.589

Crop field trials and residue decline						PMRA No. 3161375, 3161379, 3436654, 3436651, 3161377, 3436656, 3436655, 3161378, 3436653, 3436647, 3436652, 3436650, 3436648, 3436649, 3161376			
			Combined[2]		1.568	9.624	3.861	4.163	2.484
Mustard greens	539-551	1-8	Spiropidion	4	0.013	0.649	0.194	0.262	0.274
			SYN547305		2.716	4.017	3.291	3.329	0.600
			Combined[2]		2.870	4.030	3.733	3.591	0.512
Broccoli	534-542	1-10	Spiropidion	8	0.011	0.205	0.039	0.077	0.077
			SYN547305		1.030	8.519	3.213	4.187	2.704
			Combined[2]		1.208	8.533	3.229	4.264	2.678
Cabbage (With Wrapper Leaves)	534-555	1-10	Spiropidion	8	<0.010	0.426	0.033	0.132	0.160
			SYN547305		0.162	2.142	1.032	1.055	0.714
			Combined[2]		0.193	2.427	1.089	1.186	0.817
Cauliflower	524-550	1-10	Spiropidion	8	<0.010	0.277	0.017	0.074	0.110
			SYN547305		0.128	2.251	0.749	0.923	0.789
			Combined[2]		0.138	2.261	0.767	0.998	0.789
Brussels sprouts	537-554	1-11	Spiropidion	5	<0.010	0.126	0.053	0.054	0.045
			SYN547305		0.150	0.935	0.493	0.594	0.331
			Combined[2]		0.203	0.945	0.619	0.648	0.309
Tomato (field)	530-565	1-10	Spiropidion	18	0.012	0.251	0.036	0.067	0.073
			SYN547305		<0.010	0.343	0.100	0.125	0.097
			Combined[2]		0.029	0.503	0.170	0.192	0.131
Tomato (GH)	537-557	1-20	Spiropidion	5	0.017	0.412	0.087	0.160	0.158
			SYN547305		0.053	0.229	0.084	0.108	0.070
			Combined[2]		0.090	0.512	0.142	0.265	0.196
Tomato (combined field + GH)	530-565	1-20	Spiropidion	23	0.012	0.412	0.044	0.088	0.100
			SYN547305		<0.010	0.343	0.101	0.122	0.091
			Combined[2]		0.029	0.512	0.157	0.208	0.146
Bell pepper (field)	539-563	1	Spiropidion	9	0.013	0.085	0.058	0.053	0.025
			SYN547305		0.054	0.445	0.244	0.231	0.138
			Combined[2]		0.106	0.493	0.326	0.284	0.133
Bell pepper (GH)	545-565	1-21	Spiropidion	3	0.105	0.193	0.126	0.141	0.046
			SYN547305		0.088	0.170	0.156	0.138	0.044
			Combined[2]		0.214	0.349	0.275	0.279	0.067
Bell pepper (combined field + GH)	539-565	1-21	Spiropidion	12	0.013	0.193	0.068	0.075	0.049
			SYN547305		0.054	0.445	0.196	0.209	0.125
			Combined[2]		0.106	0.493	0.309	0.283	0.117
Non-bell pepper (field)	534-554	1-11	Spiropidion	10	0.018	0.253	0.053	0.095	0.088
			SYN547305		0.047	0.480	0.171	0.188	0.131
			Combined[2]		0.073	0.693	0.257	0.282	0.192
	549-554	1	Spiropidion	2	0.058	0.357	0.208	0.208	0.211

Crop field trials and residue decline						PMRA No. 3161375, 3161379, 3436654, 3436651, 3161377, 3436656, 3436655, 3161378, 3436653, 3436647, 3436652, 3436650, 3436648, 3436649, 3161376			
Non-bell pepper (GH)			SYN547305		0.281	0.459	0.370	0.370	0.126
			Combined[2]		0.517	0.638	0.577	0.577	0.086
Non-bell pepper (combined field + GH)	534-554	1-11	Spiropidion	12	0.018	0.357	0.067	0.114	0.111
			SYN547305		0.047	0.480	0.208	0.218	0.143
			Combined[2]		0.073	0.693	0.289	0.332	0.210
Eggplant	537-550	1	Spiropidion	4	<0.010	0.018	0.013	0.014	0.004
			SYN547305		0.052	0.897	0.510	0.492	0.419
			Combined[2]		0.069	0.915	0.520	0.506	0.419
Cucumber (field)	532-550	1	Spiropidion	9	<0.010	0.090	0.015	0.024	0.026
			SYN547305		<0.100	0.424	0.254	0.240	0.120
			Combined[2]		0.115	0.440	0.264	0.264	0.109
Cucumber (GH)	520-572	1-7	Spiropidion	5	0.011	0.143	0.022	0.043	0.056
			SYN547305		0.081	1.016	0.460	0.445	0.371
			Combined[2]		0.105	1.038	0.532	0.488	0.378
Cucumber (combined field + GH)	520-572	1-7	Spiropidion	14	<0.010	0.143	0.016	0.031	0.038
			SYN547305		0.081	1.016	0.272	0.313	0.248
			Combined[2]		0.105	1.038	0.282	0.344	0.252
Cantaloupe	536-558	1	Spiropidion	9	0.012	0.082	0.044	0.044	0.022
			SYN547305		0.088	0.466	0.157	0.227	0.150
			Combined[2]		0.117	0.526	0.201	0.271	0.148
Summer squash	531-545	1	Spiropidion	8	<0.010	0.020	0.011	0.012	0.003
			SYN547305		0.047	0.333	0.227	0.210	0.114
			Combined[2]		0.060	0.343	0.238	0.223	0.114
Orange (dilute spray)	490-499	1-10	Spiropidion	8	0.012	0.237	0.110	0.107	0.084
			SYN547305		0.050	0.198	0.098	0.110	0.053
			Combined[2]		0.095	0.393	0.179	0.217	0.122
Orange (concentrate spray)	492-505	1	Spiropidion	7	0.059	1.275	0.255	0.368	0.410
			SYN547305		0.026	0.121	0.045	0.063	0.037
			Combined[2]		0.085	1.377	0.305	0.431	0.431
Grapefruit (dilute spray)	495-502	1	Spiropidion	3	0.049	0.074	0.062	0.062	0.012
			SYN547305		0.042	0.072	0.061	0.058	0.015
			Combined[2]		0.116	0.123	0.122	0.120	0.004
Grapefruit (concentrate spray)	493-498	1	Spiropidion	3	0.035	0.164	0.071	0.090	0.067
			SYN547305		0.017	0.076	0.028	0.040	0.032
			Combined[2]		0.088	0.192	0.111	0.130	0.055
	492-499	1-11	Spiropidion	3	0.012	0.084	0.077	0.058	0.040
			SYN547305		<0.010	0.056	0.046	0.038	0.024

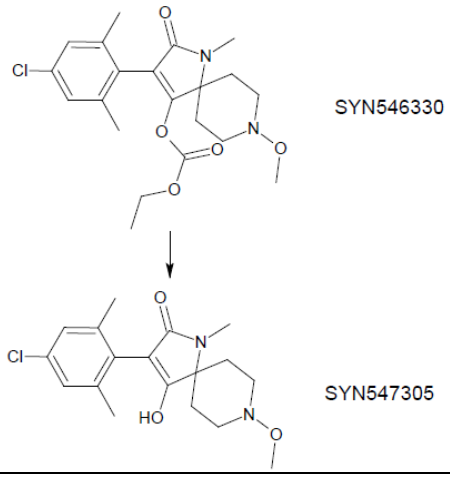
Crop field trials and residue decline						PMRA No. 3161375, 3161379, 3436654, 3436651, 3161377, 3436656, 3436655, 3161378, 3436653, 3436647, 3436652, 3436650, 3436648, 3436649, 3161376			
Lemon (dilute spray)			Combined[2]		0.022	0.132	0.124	0.092	0.061
Lemon (concentrate spray)	494-495	1	Spiropidion	2	0.012	0.371	0.192	0.192	0.254
			SYN547305		0.072	0.113	0.093	0.093	0.029
			Combined[2]		0.083	0.483	0.283	0.283	0.283
Apple (dilute spray)	593-609	20-21	Spiropidion	8	0.012	0.187	0.030	0.053	0.060
			SYN547305		<0.010	0.061	0.037	0.035	0.017
			Combined[2]		0.027	0.226	0.071	0.088	0.067
Apple (concentrate spray)	594-617	20-28	Spiropidion	8	0.024	0.193	0.068	0.085	0.064
			SYN547305		0.011	0.095	0.032	0.043	0.033
			Combined[2]		0.036	0.237	0.127	0.124	0.069
Pear (dilute spray)	600-616	21	Spiropidion	4	<0.010	0.065	0.030	0.034	0.027
			SYN547305		<0.010	0.020	0.012	0.013	0.005
			Combined[2]		<0.020	0.084	0.042	0.047	0.029
Pear (concentrate spray)	597-614	21-28	Spiropidion	4	<0.010	0.239	0.055	0.090	0.106
			SYN547305		<0.010	0.018	0.010	0.012	0.004
			Combined[2]		0.028	0.249	0.065	0.102	0.104
Grape	598-628	14-28	Spiropidion	16	0.056	0.816	0.170	0.244	0.216
			SYN547305		0.015	0.681	0.103	0.184	0.189
			Combined[2]		0.071	1.497	0.354	0.428	0.348
Cotton seed	437-448	12-28	Spiropidion	14	<0.010	0.155	0.014	0.046	0.054
			SYN547305		0.013	0.333	0.063	0.098	0.094
			Combined[2]		0.036	0.345	0.142	0.144	0.097
Soybean seed	348-375	10-18	Spiropidion	21	<0.01	0.016	<0.010	0.011	0.002
			SYN547305		<0.01	1.755	0.328	0.455	0.405
			Combined[2]		0.02	1.765	0.343	0.466	0.405

n = number of independent trials
[1] Expressed as parent equivalents.
[2] The combined residues include spiropidion and metabolite SYN547305, expressed as parent equivalents.
For computation, values <LOQ are assumed to be at the LOQ.

High-temperature hydrolysis study	PMRA No. 3161382, 3161383, 3161384, 3161381
The radiolabelled test compounds [Phenyl-U-14C]-Spiropidion and [Phenyl-U-14C]-SYN547305 were used for hydrolysis investigations with a concentration range of approximately 0.94–0.98 mg a.i./L, and 0.902–1.011 mg a.i./L, respectively. As the pH and hydrolysis temperature increases, spiropidion degrades into SYN547305, while that of the metabolite SYN547305 is considered to be hydrolytically stable and no other radiolabelled components were identified.	

High-temperature hydrolysis study			PMRA No. 3161382, 3161383, 3161384, 3161381
[Phenyl-U-14C]-Spiropidion			
Processing	**Pasteurization**	**Baking/brewing/boiling**	**Sterilization**
Conditions	**pH 4/90°C/20 min**	**pH 5/100°C/60 min**	**pH 6/120°C/20 min**
Major identified metabolites (% of Radioactivity)	Spiropidion (83.4-86.8%) SYN547305 (8.3-11.4%)	Spiropidion (78.2-81.3%) SYN547305 (15.9-16.5%)	Spiropidion (12.8-15.2%) SYN547305 (84.8-85.7%)
[Phenyl-U-14C]-SYN547305			
Processing	**Pasteurization**	**Baking/brewing/boiling**	**Sterilization**
Conditions	**pH 4/90°C/20 min**	**pH 5/100°C/60 min**	**pH 6/120°C/20 min**
Major identified metabolites (% of Radioactivity)	SYN547305 (98.1-99.5%)	SYN547305 (98.1-99.2%)	SYN547305 (96.3-98.1%)

Proposed hydrolysis scheme



Processed food and feed – Potatoes, soybeans, tomatoes, apple, orange, grape, cotton					PMRA No. 3161375, 3161376, 3161377, 3436657, 3436647, 3436658, 3436648	
Processing studies were conducted at exaggerated rates (up to fivefold GAP) on potatoes, soybeans, cotton, apples, grapes, tomatoes and oranges during the 2017 and 2020 growing seasons, using spiropidion (A20262B; containing 300 g a.i./L; SC). 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.						
RAC	**Spiropidion HAFT[RAC] (ppm)**	**SYN547305 HAFT[RAC] (ppm)**	**Processed fractions**	**Median processing factor of spiropidion**	**Median processing factor of SYN547305**	**Anticipated residues[1] (ppm)**
Potato	0.01	0.886	Boiled with skin	NC	0.90	0.80

Processed food and feed – Potatoes, soybeans, tomatoes, apple, orange, grape, cotton					**PMRA No. 3161375, 3161376, 3161377, 3436657, 3436647, 3436658, 3436648**	
			Microwaved with skin	NC	0.54	0.48
			Baked with skin	NC	1.69	1.50
			Pan fried	NC	0.47	0.42
			Chips	NC	0.77	0.68
			Fries	NC	1.43	1.27
			Flakes	NC	3.49	3.10
			Starch	NC	0.15	0.13
			Protein	NC	6.94	6.15
Soybean	0.016	1.755	Refined oil	NC	NC	0.02
			Flour	NC	1.60	2.82
			Soy milk	NC	0.07	0.12
			Tofu	NC	0.10	0.18
			Soy sauce	NC	0.01	0.02
			Miso	NC	0.16	0.28
Tomato	0.251	0.343	Juice	0.30	1.00	0.42
			Preserved/canned	0.30	0.70	0.32
			Paste	0.30	3.7	1.34
			Purée	0.30	1.7	0.66
			Dried tomato	2.90	12.2	4.91
Apple	0.193	0.095	Juice	0.20	0.60	0.10
			Apple sauce	0.01	0.10	0.01
			Canned apple	0.01	0.10	0.01
			Jelly	0.01	0.20	0.02
			Dried apple	0.01	1.10	0.11
Orange	1.275	0.121	Peel	0.70	2.70	1.22
			Juice	0.20	0.20	0.28
			Oil	73.30	0.30	93.49
Grape	0.816	0.681	Juice (red)	0.80	1.50	1.67
			Juice (white)	0.50	1.30	1.29
			Jelly	0.20	0.60	0.57
			Aged wine (red)	0.70	5.20	4.11
			Aged wine (white)	0.20	1.40	1.12
			Must	1.80	1.50	2.49
			Raisins	2.10	2.20	3.21
Cotton	0.155	0.333	Refined oil	0.02	0.04	0.02

NC = Not calculated (<LOQ). For computation, values <LOQ are assumed to be at the LOQ.
[1] Anticipated residues (AR) = (Spiropidion HAFT × PF) + (SYN547305 HAFT × PF).

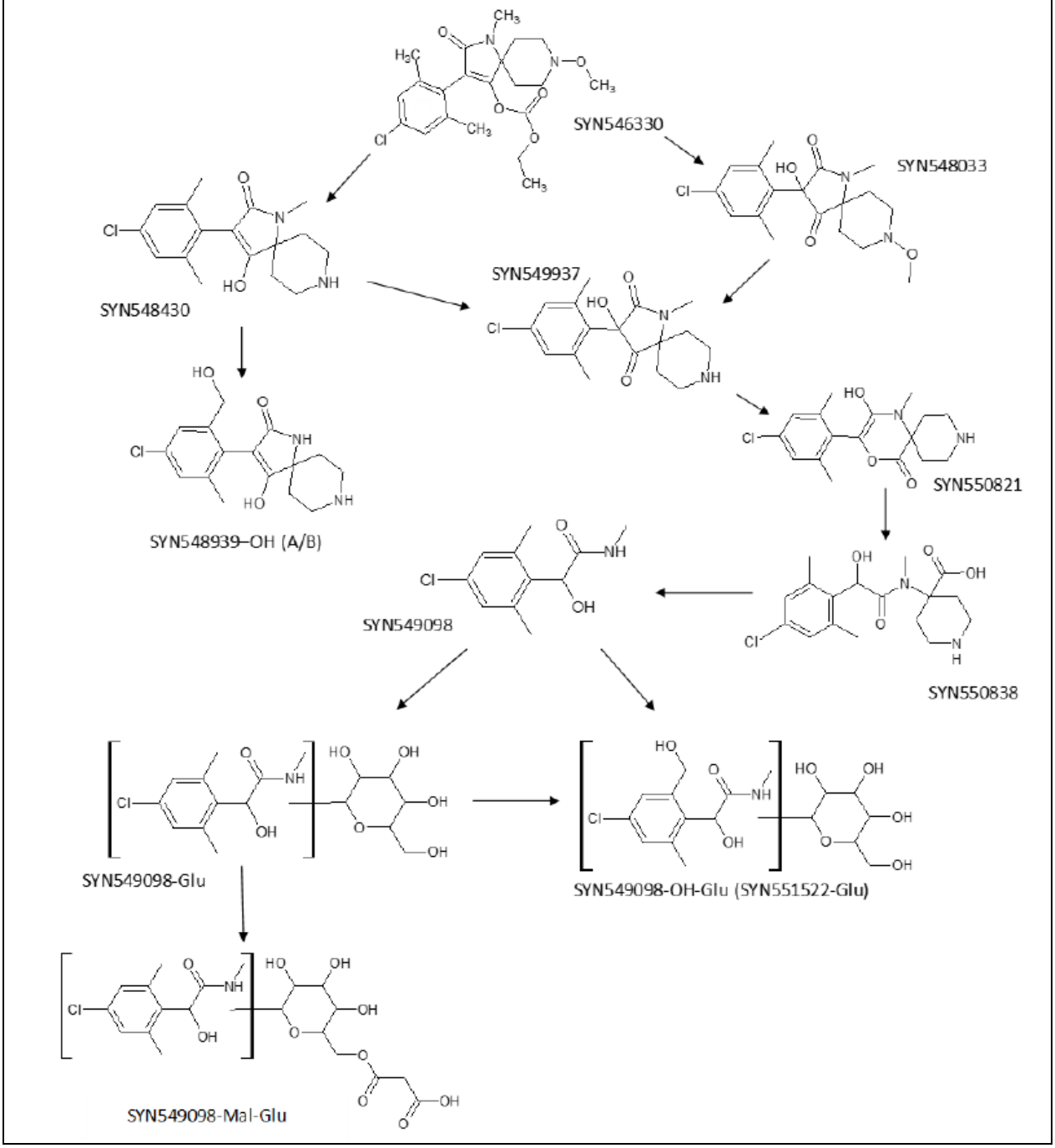
Confined accumulation in rotational crops – Wheat, lettuce, turnip	PMRA No. 3436659
Radiolabel position	[phenyl-U-14C] (specific activity: 2.98 or 3.04 MBq/mg); [spirodecanone-5-14C] (specific activity: 2.92 or 2.94 MBq/mg)
Treatment	
Test site	Individual containers were filled with 10 cm of polystyrene packaging chips and the remainder with soil. These containers were set up indoors for test item application and then moved outdoors to provide initial period of outdoor exposure. After three days, the containers were brought into separate glasshouses.
Soil type	Sandy loam
Treatment	Bare soil was treated at 590.4 g a.i./ha and 588.0 g a.i./ha for phenyl-14C and spiro-14C, respectively. The soil was aged for 30, 120 and 275 days, prior to planting wheat, lettuce and turnip.
Formulation	Suspension concentrate (SC) formulation of spiropidion (guarantee: 300 g/L).
Extraction solvents	Samples of rotational crop commodities with TRR ≥0.01 ppm were extracted 2-3× with ACN:water (4:1; v/v), then once with ACN:water (1:1; v/v). Samples of hay and straw were soaked in water for ~30 minutes prior to extraction. The extracts were combined, concentrated if needed, then reconstituted in ACN:water (4:1 or 1:1; v/v) prior to HPLC and TLC analysis. Extracts of wheat straw (120-day PBI, phenyl only) and immature lettuce (120-day PBI, phenyl) underwent an additional hydrolysis step prior to HPLC analysis. Wheat straw (120d PBI, phenyl label only): An aliquot of the combined extract was hydrolyzed in 2M HCl in a water bath (60°C for 2 hours). The sample was then neutralized with diluted NaOH prior to analysis. These steps were repeated for an additional hydrolysis step (except with the water bath heated up to 90°C). Immature lettuce (120d PBI, phenyl): 0.05M NaOH was added to the extract and then incubated at room temperature for 24 hours, concentrated to dryness, dissolved in pH 4 acetate buffer, followed by sonication. Pectinase solution was added, and the sample was centrifuged, the supernatant decanted and made up to a known volume. Aliquots of the sample were concentrated and reconstituted in 1M HCl. One aliquot was heated to 60°C for 4 hours, the other was heated to 90°C for 4 hours. The samples were then concentrated reconstituted in acetonitrile:water (1:1; v/v) prior to HPLC analysis.

Confined accumulation in rotational crops – Wheat, lettuce, turnip			PMRA No. 3436659
Radiolabel position	**Total radioactive residues (ppm)**		
	[Phenyl-14C]/[Spiro-14C]		
Matrices	**1st Rotation (30-day PBI)**	**2nd Rotation (120-day PBI)**	**3rd Rotation (275-day PBI)**
Wheat forage	0.075 – 0.208	0.051 – 0.080	0.014 – 0.104
Wheat hay	0.253 – 0.344	0.097 – 0.241	0.030 – 0.175
Wheat straw	0.268 – 0.630	0.318 – 0.644	0.059 – 0.225
Wheat grain	0.014 – 0.021	0.025 – 0.027	0.008
Immature lettuce	0.032 – 0.067	0.042 – 0.085	0.011 – 0.033
Mature lettuce	0.010 – 0.031	0.022	NE
Turnip foliage	0.034 – 0.053	0.028	0.029
Turnip root	NE	NE	NE

NE = Not extracted.

Summary of major identified metabolites in rotated crops			
Radiolabel position	**[Phenyl-14C]/[Spiro-14C]**		
Plant-back intervals (PBI)	**1st Rotation (30-day PBI)**	**2nd Rotation (120-day PBI)**	**3rd Rotation (275-day PBI)**
Wheat forage	SYN548033 SYN549937 SYN550821	SYN549098 SYN548939-OH A SYN549937	SYN549098 SYN548939-OH A SYN548939-OH B
Wheat hay	-	SYN552982	SYN549098 SYN552982 SYN548939-OH A SYN548939-OH B
Wheat straw	-	SYN548033	SYN549098 SYN552982 SYN548939-OH A SYN548939-OH B
Wheat grain	SYN548430	-	-
Immature lettuce	SYN548033	SYN549098 SYN549098-Mal-Glu SYN548033 SYN550838 SYN548939-OH A SYN548939-OH B	SYN549098 SYN549098-Mal-Glu SYN548033 SYN548939-OH A SYN548939-OH B
Mature lettuce	SYN549098-Mal-Glu SYN548033	SYN549098 SYN549098-Mal-Glu	-
Turnip foliage	SYN549098-Glu SYN548430 SYN549937	SYN549098 SYN549098-Glu SYN549098-Mal-Glu	SYN549098 SYN549098-Mal-Glu SYN549098-Glu

Proposed metabolic scheme in rotational crops



Residue data in rotational crops	PMRA No. 3436667

Thirty-eight trials (14 trials for wheat; 8 trials for mustard and turnip; 4 trials for lettuce and carrot) were conducted during the 2020-2021 growing season in North American growing regions. Three pre-plant broadcast spray applications were made to bare soil with A20262B at a rate of ~180 g a.i./ha/application, with retreatment intervals of 5-9 days, for a maximum rate of 534-587 g a.i./ha. No adjuvants were used in the study. Rotational crops were planted at four different plant-back intervals of 28-31, 89-93, 179-190, and 265-271 days. Adequate storage stability data are available on diverse commodity categories to support the storage intervals of the rotational crop field trials. Samples were analyzed using a validated analytical method.

Commodity	Total application rate (g a.i./ha)	PBI (days)	Residue levels (ppm)						
			Analyte	n	LAFT	HAFT	Median	Mean	SDEV
Mustard leaves	559-567	28	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-576	89-90	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	546-557	180-182	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	557-587	268-271	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Turnip leaves	559-575	28	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-581	89-90	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-557	180-182	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-577	268-271	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Turnip roots	559-575	28	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-581	89-90	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-557	180-182	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	553-577	268-271	Spiropidion	2	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Wheat forage	541-546	29-31	Spiropidion	5	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	544-581	89-93	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	546-553	181-183	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	540-576	265-271	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Wheat hay	541-546	29-31	Spiropidion	5	<0.01	<0.01	<0.01	<0.01	-

Residue data in rotational crops								PMRA No. 3436667	
			SYN549098[1]		<0.01	0.019	<0.01	0.012	0.0040
	544-581	89-93	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	546-553	181-183	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	540-576	265-271	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Wheat grain	541-546	29-31	Spiropidion	5	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	544-581	89-93	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	546-553	181-183	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	540-576	265-271	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Wheat straw	541-546	29-31	Spiropidion	5	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	544-581	89-93	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	546-553	181-183	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	540-576	265-271	Spiropidion	3	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Lettuce	546	31	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	540	91	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	544	190	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	548	269	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Carrot leaves	546	30	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	535	90	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	547	179	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	548	268	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
Carrot roots	546	30	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	535	90	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	547	179	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-

Residue data in rotational crops									PMRA No. 3436667
			SYN549098		<0.01	<0.01	<0.01	<0.01	-
	548	268	Spiropidion	1	<0.01	<0.01	<0.01	<0.01	-
			SYN549098		<0.01	<0.01	<0.01	<0.01	-

1 Measurable residues of SYN549098 were expressed in parent equivalents using a molecular weight ratio of 1.86

Table 15 Food residue chemistry overview of metabolism studies and risk assessment

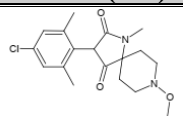
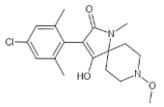
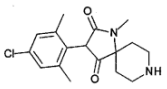
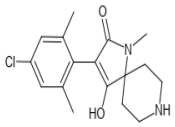
Plant studies	
Residue definition for enforcement	
Primary crops (tomato, cotton, potato)	Spiropidion and its metabolite SYN547305, expressed as spiropidion equivalents.
Rotational crops (lettuce, wheat, turnip)	Spiropidion and its metabolite SYN549098 (free and conjugated), expressed as spiropidion equivalents.
Residue definition for risk assessment	
Primary crops (tomato, cotton, potato)	Spiropidion and its metabolites SYN547305, SYN547435, and SYN548430, expressed as spiropidion equivalents.
Rotational crops (lettuce, wheat, turnip)	Spiropidion and its metabolite SYN549098 (free and conjugated) and SYN550838, expressed as spiropidion equivalents.
Metabolic profile in diverse crops	
Similar metabolism has been demonstrated in tomato, cotton, and potato (primary crops) and lettuce, wheat and turnip (rotational crops).	
Animal studies	
Residue definition for enforcement	Not determined as part of this submission.
Residue definition for risk assessment	

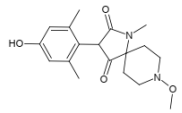
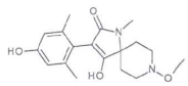
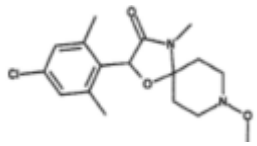
Dietary risk from food and drinking water			
Refined acute dietary exposure analysis, 95th percentile **ARfD = 0.3 mg/kg bw (general population)** **= 0.03 mg/kg bw (females 13-49 years)**	**Population**	**Estimated risk** **% of acute reference dose (ARfD)**	
		Food alone	**Food and drinking water**
	All Infants	9.1	10.4
	Children 1–2 years	18.8	19.2

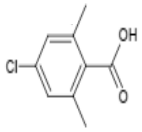
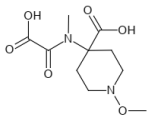
Estimated acute drinking water concentration = 0.033 ppm	Children 3–5 years	14.2	14.3
	Children 6–12 years	7.8	8.1
	Males 13–49 years	5.5	5.7
	Adults 50+ years	7.3	7.7
	Females 13-49 years	**76.3**	**77.9**
Refined chronic dietary exposure analysis **ADI = 0.03 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.017 ppm**	**Population**	**Estimated risk % of acceptable daily intake (ADI)**	
		Food alone	**Food and drinking water**
	General Population	6.7	7.8
	All Infants	8.5	12.8
	Children 1–2 years	**18.6**	**20.2**
	Children 3–5 years	13.5	14.8
	Children 6–12 years	7.6	8.6
	Youth 13–19 years	4.4	5.2
	Adults 20–49 years	5.7	6.8
	Adults 50+ years	6.4	7.5

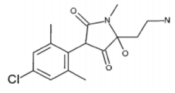
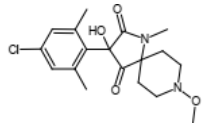
Table 16 Summary of the major transformation products of spiropidion in the environment

Major transformation product (TP)[(1)]	Maximum mean concentration in spiropidion environmental fate studies[(2)]	Comments
Major TP 1: SYN547305 **IUPAC:** 2-(4-chloro-2,6-dimethyl-phenyl)-1-hydroxy-8-methoxy-4-methyl4,8-diazaspiro[4.5]dec-1-en-3-one	Hydrolysis: **96.8% AR** Phototransformation on dry soil: **22.6% AR** (irradiated); **33.2% AR** (dark) Phototransformation on moist soil: **47.6% AR** (irradiated); **61.5% AR** (dark) Aqueous phototransformation in pH 5 buffer solution: 8.68% AR (irradiated), **54.9% AR** (dark)	SYN547305 is the first TP formed in the transformation of spiropidion. It is a major TP in all environmental fate studies. SYN547305 can undergo keto–enol tautomerism.

Major transformation product (TP)[1]	Maximum mean concentration in spiropidion environmental fate studies[2]	Comments
 Keto tautomer  Enol tautomer $C_{18}H_{23}ClN_2O_3$ MW: 350.9 g/mol	Aqueous phototransformation in natural water: 6.20% AR (irradiated), **99.4% AR** (dark) Aerobic biotransformation in soil: **71.5% AR** Anaerobic biotransformation in soil: **72.1% AR** Aerobic aquatic biotransformation: **92.1% AR** Anaerobic aquatic biotransformation: **87.9% AR** Terrestrial field dissipation (TFD): **~25% applied parent** K_{oc}: 0.66 to 83.99 (10 soils)	
Major TP 2: SYN548430 IUPAC: 2-(4-chloro-2,6-dimethyl-phenyl)-4-methyl-4,8-diazaspiro[4.5]decane-1,3-dione  Keto tautomer  Enol tautomer $C_{17}H_{21}ClN_2O_2$ MW 320.8 g/mol	Hydrolysis: not detected Phototransformation on dry soil: not detected (irradiated); 0.55% AR (dark) Phototransformation on moist soil: not detected Aqueous phototransformation: not included in the chemical analysis Aerobic biotransformation in soil: 5.50% AR Anaerobic biotransformation in soil: **9.55%** AR (**10.3% AR** in one replicate) Aerobic aquatic biotransformation: **13.5% AR** Anaerobic aquatic biotransformation: **12.1% AR** TFD: <1% applied parent K_{oc}: not available	SYN548430 is a secondary TP formed from the transformation of SYN547305. It slightly exceeded 10% AR in the anaerobic biotransformation in soil study (one sample only), and the aerobic and anaerobic aquatic biotransformation studies, with the concentration still increasing at the end of the studies. It is a minor TP (<10% AR) in the other studies. SYN548430 can undergo keto–enol tautomerism.
Major TP 3: SYN548274 **IUPAC**: 4-hydroxy-3-(4-hydroxy-2,6-dimethyl-phenyl)-8-methoxy-1-methyl-1,8-diazaspiro[4.5]dec-3-en-2-one	Hydrolysis: not included in chemical analysis Phototransformation on dry soil: 1.00% AR (irradiated); 1.05% AR (dark) Phototransformation on moist soil: 0.43% AR (irradiated), 6.50% AR (dark)	SYN548274 is a secondary TP formed from the transformation of SYN547305. It was only observed in the aqueous phototransformation studies (irradiated samples only) as a result of the

Major transformation product (TP)[1]	Maximum mean concentration in spiropidion environmental fate studies[2]	Comments
 Keto tautomer  Enol tautomer $C_{18}H_{24}N_2O_4$ MW 332.4 g/mol	Aqueous phototransformation in pH 5 buffer solution: **23.6% AR** (irradiated), not detected (dark) Aqueous phototransformation in natural water: **49.9% AR** (irradiated), not detected (dark) Aerobic biotransformation in soil: not detected Anaerobic biotransformation in soil: not included in chemical analysis Aerobic aquatic biotransformation: not included in chemical analysis Anaerobic aquatic biotransformation: not detected TFD: not included in chemical analysis K_{oc}: not available	phototransformation of SYN547305. SYN548274 can undergo keto–enol tautomerism.
Major TP 4: SYN552045 IUPAC: 2-(4-chloro-2,6,-dimethyl-phenyl)-8-methoxy-4-methyl-1-oxa-4,8-diazaspiro[4.5]decan-3-one  $C_{17}H_{23}ClN_2O_2$ MW 338.8 g/mol	Hydrolysis: not included in chemical analysis Phototransformation on dry soil: not detected Phototransformation on moist soil: 9.00% AR (**11.6% AR in one replicate**; irradiated), <1.38% AR (dark) Aqueous phototransformation: not included in chemical analysis Aerobic biotransformation in soil: not included in chemical analysis Anaerobic biotransformation in soil: not included in chemical analysis Aerobic aquatic biotransformation: not included in chemical analysis Anaerobic aquatic biotransformation: not included in chemical analysis TFD: <1% applied K_{oc}: 76.6 to 115 (three soils)	SYN552045 is a secondary TP formed from the transformation of SYN547305. In the laboratory, it was only included in the chemical analysis package for the phototransformation on soil study, where it was produced as a result of the transformation of SYN547305. It slightly exceeded 10% AR in several samples; however, mean values were <10% AR. It was measured at <1% applied parent in the TFD.
Major TP 5: SYN548037 IUPAC: **4-chloro-2,6-dimethyl-benzoic acid**	Hydrolysis: not included in chemical analysis Phototransformation on dry soil: <1.95% AR (irradiated), <1.7% AR (dark)	SYN548037 is produced following the transformation of several TPs (SYN547305 to SYN548033 to SYN550839 to SYN549098). In the

Major transformation product (TP)[1]	Maximum mean concentration in spiropidion environmental fate studies[2]	Comments
 $C_9H_9ClO_2$ MW 184.6 g/mol	Phototransformation on moist soil: **10.65% AR** (irradiated), not detected (dark) Aqueous phototransformation: not included in chemical analysis Aerobic biotransformation in soil: not detected Anaerobic biotransformation in soil: not detected Aerobic aquatic biotransformation: not detected Anaerobic aquatic biotransformation: not detected TFD: <1% applied K_{oc}: 1.89 to 5.54 (three soils)	laboratory, it was only observed in the soil phototransformation study, at concentrations slightly exceeding 10% AR (concentration increasing at the end of the study) as a result of the phototransformation of SYN547305. It was measured at <1% applied parent in the TFD.
Major TP 6: SYN551480 1-methoxy-4-[methyl (oxalo) amino] piperidine-4-carboxylic acid  $C_{10}H_{16}N_2O_6$ MW 260.246 g/mol	Hydrolysis: not included in chemical analysis Phototransformation on soil: not included in chemical analysis Aqueous phototransformation in pH 5 buffer solution: not identified (only identified compounds present at >10% AR) Aqueous phototransformation in natural water: **12.2% AR** (irradiated), not identified (dark) Aerobic biotransformation in soil: not included in chemical analysis Anaerobic biotransformation in soil: not included in chemical analysis Aerobic aquatic biotransformation: not included in chemical analysis Anaerobic aquatic biotransformation: not included in chemical analysis TFD: not included in chemical analysis K_{oc}: not available	SYN551480 is a secondary TP formed from the transformation of SYN547305. It was only included in the chemical analysis package for the aqueous phototransformation study.
Major TP 7: SYN552257 IUPAC: 5-(2-aminoethyl)-3-(4-chloro-2,6-dimethyl-phenyl)-5-hydroxy-1-	Hydrolysis: not included in chemical analysis Phototransformation on dry soil: not detected Phototransformation on moist soil: 1.68% AR (irradiated), 3.85% AR (dark)	SYN552257 is a secondary TP produced in aerobic soil from the transformation of SYN547305. In the laboratory, it slightly exceeded 10% AR in one soil only (max. 15.2% AR

Major transformation product (TP)[1]	Maximum mean concentration in spiropidion environmental fate studies[2]	Comments
methyl-pyrrolidine-2,4-dione  $C_{15}H_{19}ClN_2O_3$ MW 310.8 g/mol	Aqueous phototransformation: not included in chemical analysis Aerobic biotransformation in soil: **13.58% AR** Anaerobic biotransformation in soil: not included in chemical analysis Aerobic aquatic biotransformation: not included in chemical analysis Anaerobic aquatic biotransformation: not identified TFD: <1% applied parent K_{oc}: 2.436 to 12.37 (three soils)	in one replicate). It was measured at <1% applied parent in the TFD. It was not included in the chemical analysis for the biotransformation in anaerobic soil or aerobic aquatic biotransformation studies.
Major TP 8: SYN548033 **IUPAC:** [2-(4-chloro-2,6-dimethyl-phenyl)-2-hydroxy-8-methoxy-4,8-diazaspiro[4.5]decane-1,3-dione]  $C_{18}H_{23}ClN_2O_4$ MW: 366.8 g/mol	Hydrolysis: not included in chemical analysis Phototransformation on dry soil: 2.38% AR (both irradiated and dark) Phototransformation on moist soil: 2.77% AR (irradiated), 3.60% AR (dark) Aqueous phototransformation: not included in chemical analysis Aerobic biotransformation in soil: 5.17% AR Anaerobic biotransformation in soil: 4.43% AR Aerobic aquatic biotransformation: 3.00% AR Anaerobic aquatic biotransformation: 3.70% AR TFD: **~10-15%** applied parent K_{oc}: 54.94 to 70.94 (three soils)	SYN548033 is a secondary TP formed from the transformation of SYN547305. It was formed at approximately 10-15% of applied parent in the field but was a minor TP in the laboratory studies.

>10% AR or >10% applied parent bolded

(1) The environmental fate studies used ^{14}C-spiropidion, with radiolabels on the spiro and phenyl rings of the molecule.

(2) The maximum mean concentration of both radiolabels is presented, unless otherwise indicated.

Table 17 Fate and behaviour of spiropidion in the environment

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
Abiotic transformation							
Hydrolysis	Spiropidion (SYN546330; technical grade active ingredient)	pH 4 buffer, 25ºC	t_R/DT_{50} = 11.4 days	SFO	SYN547305	Hydrolysis is an important transformation process for spiropidion, especially at pH 9.	3436710
		pH 4 buffer, 35ºC	t_R/DT_{50} = 6.17 days				
		pH 4 buffer, 50ºC	t_R/DT_{50} = 2.51 days				
		pH 7 buffer, 15ºC	t_R/DT_{50} = 15.8 days				
		pH 7 buffer, 25ºC	t_R/DT_{50} = 5.35 days				
		pH 7 buffer, 50ºC	t_R/DT_{50} = 1.88 days				
		pH 9 buffer, 15ºC	t_R/DT_{50} = 0.35 days				
		pH 9 buffer, 25ºC	t_R/DT_{50} = 0.10 days				
		pH 9 buffer, 35ºC	t_R/DT_{50} = 0.04 days				
Phototransformation on soil		Phototransformation is a negligible process for spiropidion; however, under irradiated conditions, SYN547305 is transformed into SYN548274 by oxidative dechlorination, followed by cleavage to SYN551480.					3436672
Phototransformation in water							3436711
Phototransformation in air	N/A – volatilization of spiropidion and its major TPs in the field is expected to be negligible.						
Biotransformation							
Biotransformation in aerobic soil[2]	Spiropidion (SYN546330; technical	Marsillargues (silty clay; pH 7.8, 1.0%	**Spiropidion** t_R = 0.78 days DT_{50} = 0.33 days	DFOP	SYN547305 Non-extractable residues	Spiropidion is non-persistent in the tested soils.	3436669

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[(1)]	Comments	PMRA No.
	grade active ingredient)	organic carbon (OC))	**SYN547305** t_R/ DT_{50} = 5.16 days	SFO	CO_2	SYN547305 is non-persistent in all tested soils, except in Marsillargues soil, where it is slightly persistent. SYN552257 was a major TP in Capay soil only, where it was slightly persistent.	
		18 Acres (sandy clay loam; pH 5.9, 2.6% OC)	**Spiropidion** t_R = 1.61 days DT_{50} = 1.11 days **SYN547305** t_R = 6.68 days DT_{50} = 4.15 days	IORE IORE	SYN547305 Non-extractable residues CO_2		
		Gartenacker (loam; pH 7.3, 2.3% OC)	**Spiropidion** t_R = 0.65 days DT_{50} = 0.26 days **SYN547305** t_R/DT_{50} = 2.19 days	IORE SFO	SYN547305 Non-extractable residues CO_2		
		Hepler (silt loam; pH 5.6, 3.8% OC)	**Spiropidion** t_R = 1.56 days DT_{50} = 0.72 days **SYN547305** t_R = 11.5 days DT_{50} = 2.88 days	IORE IORE	SYN547305 Non-extractable residues CO_2		
		Capay (clay loam pH 7.7, 1.0% OC)	**Spiropidion** t_R = 1.30 days DT_{50} = 0.75 days **SYN547305** t_R/DT_{50} = 4.29 days	IORE SFO	SYN547305 SYN552257 Non-extractable residues CO_2		

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
			SYN552257 t_R/DT_{50} = 32.5 days	SFO			
Biotransformation in anaerobic soil	Spiropidion (SYN546330; technical grade active ingredient)	18 Acres (sandy clay loam, pH 5.6, 2.3% OC)	**Spiropidion** t_R = 0.95 days DT_{50} = 0.51 days **SYN547305** t_R/DT_{50} = 165 days	IORE SFO	SYN547305 Non-extractable residues	Spiropidion was non-persistent in the tested anerobic soils while SYN547305 was moderately persistent to persistent.	3436671
		Hepler (silt loam/silty clay loam, pH 5.7, 4.4% OC)	**Spiropidion** t_R = 2.19 days DT_{50} = 0.71 days **SYN547305** t_R/DT_{50} = 195 days	IORE SFO	SYN547305 Non-extractable residues		
		Gartenacker (loam, pH 7.7, 1.0% OC)	**Spiropidion** t_R/DT_{50} = 0.52 days **SYN547305** t_R/DT_{50} = 270 days	SFO SFO	SYN547305 Non-extractable residues		
		Marsillargues (silty clay; pH 7.7, 1.0% OC)	**Spiropidion** t_R = 0.57 days DT_{50} = 0.29 days **SYN547305** t_R/DT_{50} = 839 days	IORE SFO	SYN547305 Non-extractable residues		

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
Biotransformation in aerobic aquatic systems (total system)	Spiropidion (SYN546330; technical grade active ingredient)	Calwich Abbey (water: pH 7.2, TOC 7.16 mg/L; sediment: silty clay loam, pH 7.2, 6.1% OC)	**Spiropidion** t_R/DT_{50} = 2.60 days **SYN547305** t_R = 721 days DT_{50} = 485 days	SFO DFOP	SYN547305 SYN548430 Non-extractable residues	The dissolved oxygen content of the water in this study was low (generally <4 mg/L). <30% of applied radioactivity partitioned to sediment. Spiropidion was non-persistent in both systems while SYN547305 was persistent. The concentration of SYN54830 was increasing at the end of the study.	3436713
		Swiss Lake (water: pH 7.1, TOC 8.02 mg/L; sediment: sand, pH 5.1, 0.9% OC)	**Spiropidion** t_R/DT_{50} = 2.48 days **SYN547305** t_R/DT_{50} = 495 days	SFO SFO	SYN547305		
Biotransformation in anaerobic aquatic systems (total system)		Calwich Abbey (water: pH 8.7, TOC 7.16 mg/L; sediment: silty clay loam, pH 7.2, 6.1% OC)	**Spiropidion** t_R = 0.14 days DT_{50} = 0.05 days **SYN547305** t_R/DT_{50} = 305 days	IORE SFO	SYN547305 SYN548430	Low levels of oxygen were present in the water phase at various intervals throughout the study. <25% applied radioactivity partitioned to sediment. Spiropidion was non-persistent in both systems while	3436712
		Swiss Lake (water: pH 8.2, TOC 8.02 mg/L; sediment: sand, pH 5.1, 0.9% OC	**Spiropidion** t_R = 0.37 days DT_{50} = 0.07 days **SYN547305**	IORE SFO	SYN547305		

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
			t_R/DT_{50} = 498 days			SYN547305 was persistent. The concentration of SYN54830 was increasing at the end of the study.	
Bioconcentration							
Bioconcentration in fish (*Lepomis macrochirus*)	Spiropidion (SYN546330; technical grade active ingredient)	Fish	BCF_{KLG} = 53.4	N/A	N/A	BCF applies to the combined residue of spiropidion and SYN547305. More than 95% depuration was achieved after five days. Spiropidion and SYN547305 are not expected to bioaccumulate in fish	3436753
Mobility							
Adsorption/desorption in soil	Spiropidion (SYN546330; technical grade active ingredient)	Empingham (clay, pH 7.2, 5.0% OC)	K_{oc} = 71.5 mL/g K_d = 3.58 mL/g	N/A	N/A	Spiropidion is classified as having moderate to high mobility in the tested soils based on the K_{oc} values.	3436698 3436699
		Seven Springs (loamy sand, pH 5.3, 0.4% OC)	K_{oc} = 189 mL/g K_d = 0.76 mL/g				
		Hepler (silt loam, pH 5.6, 2.9% OC)	K_{oc} = 46.2 mL/g K_d = 1.34 mL/g				
		18 Acres (sandy clay loam, pH 6.0, 2.2% OC)	K_{oc} = 117 mL/g K_d = 2.57 mL/g				

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
		Capay (clay loam, pH 6.9, 0.8% OC)	K_{oc} = 270 mL/g K_d = 2.16 mL/g				
		Gartenacker (silt loam, pH 7.2, 1.8% OC)	K_{oc} = 98.1 mL/g K_d = 1.77 mL/g				
		Marsillargues (silty clay, pH 7.7, 1.0% OC)	K_{oc} = 147 mL/g K_d = 1.47 mL/g				
	SYN547305 (TP)	Empingham (clay, pH 7.2, 5.0% OC)	K_{oc} = 0.72 mL/g K_d = 0.036 mL/g	N/A	N/A	SYN547305 is classified as having very high mobility in the tested soils based on the K_{oc} values.	3436700 3436701 3436702
		Vetroz (loam, pH 7.7, 2.2% OC)	K_{oc} = 8.18 mL/g K_d = 0.18 mL/g				
		Collombey (loamy sand, pH 7.3, 2.0% OC)	K_{oc} = 9.28 mL/g K_d = 0.19 mL/g				
		Seven Springs (loamy sand, pH 5.3, 0.4% OC)	K_{oc} = 84.0 mL/g K_d = 0.34 mL/g				
		Hepler (silt loam, pH 5.6, 2.9% OC)	K_{oc} = 30.2 mL/g K_d = 0.88 mL/g				
		18 Acres (sandy clay loam, pH 6.0, 2.2% OC)	K_{oc} = 42.7 mL/g K_d = 0.94 mL/g				
		Capay (clay loam, pH 6.9, 0.8% OC)	K_{oc} = 9.43 mL/g K_d = 0.08 mL/g				

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
		Gartenacker (loam, 7.2, 1.9% OC)	K_{oc} = 4.62 mL/g K_d = 0.09 mL/g				
		Marsillargues (silty clay, pH 7.7, 1.0% OC)	K_{oc} = 0.66 mL/g K_d = 0.007 mL/g				
	SYN548037 (TP)	18 Acres (sandy loam, pH 6.0, 2.2% OC)	K_{oc} = 5.55 mL/g K_d = 0.12 mL/g	N/A	N/A	SYN548037 is classified as having very high mobility in the tested soils based on the K_{oc} values.	3436704
		Gartenacker (silt loam, pH 7.1, 2.2% OC)	K_{oc} = 1.89 mL/g K_d = 0.042 mL/g				
		Vetroz (loam, pH 7.6, 2.5% OC)	K_{oc} = 2.35 mL/g K_d = 0.059 mL/g				
	SYN552045 (TP)	Vetroz (loam, pH 7.6, 2.4% OC)	K_{oc} = 83.0 mL/g K_d = 1.99 mL/g	N/A	N/A	SYN552045 is classified as having high mobility in the tested soils based on the K_{OC} values.	3436708
		Gartenacker (loam, pH 7.2, 2.0% OC)	K_{oc} = 76.6 mL/g K_d = 1.53 mL/g				
		18 Acres (loam, pH 5.6, 2.5% OC)	K_{oc} = 115 mL/g K_d = 2.87 mL/g				
	SYN552257 (TP)	Vetroz (loam, pH 7.6, 2.4% OC)	K_{OC} = 2.50 mL/g K_d = 0.06 mL/g	N/A	N/A	SYN552257 is classified as having very high mobility in the tested soils based on the K_{oc} values.	3436709
		Gartenacker (loam, pH 7.2, 2.0% OC)	K_{oc} = 2.44 mL/g K_d = 0.049 mL/g				

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
		18 Acres (loam, pH 5.6, 2.5% OC)	K_{oc} = 12.4 mL/g K_d = 0.31 mL/g				
	SYN548033 (TP)	18 Acres (sandy loam, pH 5.6, 2.4% OC)	K_{OC} = 70.9 mL/g K_d = 1.70 mL/g	N/A	N/A	SYN548033 is classified as having high mobility in the tested soils based on the K_{OC} values.	3436703
		Gartenacker (loam, pH 7.0, 2.0% OC)	K_{oc} = 62.1 mL/g K_d = 1.24 mL/g				
		Vetroz (loam, pH 7.5, 2.1% OC)	K_{oc} = 54.9 mL/g K_d = 1.15 mL/g				
Soil leaching	Study not required or submitted.						
Volatilization	Study not required or submitted. Spiropidion is non-volatile.						
Field studies							
Terrestrial field dissipation	SYN546330 SC (A20262B, suspension concentraton formulation; 300 g a.i./ha)	Finger Lakes region, New York (loamy sand, pH 6.6-6.9, 2.0-2.2% organic matter (OM))	Spiropidion + SYN547305[3] DT_{50} = 0.96 days SYN548033 = 9.67 days Combined residue of all analytes: 1.71 days	IORE SFO	SYN547305 SYN548033	Residues of spiropidion and its TPs were non-persistent in the field. Carryover to the next growing season is not expected to be a concern. No significant downward migration of spiropidion and its TPs in soil was observed, with the majority of residues measured in the top 10 cm of the soil profile. The soil	3436686
		Minto, Manitoba (loam, pH 7.8, 2.5% OC)	Spiropidion + SYN547305[3] DT_{50} = 2.28 days SYN548033 = 7.52 days	SFO SFO	SYN547305 SYN548033		3436696

Property	Test substance	Medium	Value	Kinetic model	Major transformation products[1]	Comments	PMRA No.
			Combined residue of all analytes: 3.44 days			moisture data from the Finger Lakes and Manitoba sites show that soil moisture content was generally higher in the deeper soil layers than in the top soil layer, indicating upward water movement through capillarity. As such, water input at these sites may have been insufficient to evaluate leaching potential.	
		Wayne County, New York (loamy sand, pH 6.6-7.2, 2.1 – 2.5% OM)	Spiropidion + SYN547305[3] DT_{50} = 0.96 days Combined residue of all analytes: 1.67 days	IORE	SYN547305		3436695
Field leaching	Study not required or submitted.						

(1) Non-extractable residues are reported as a major TP as they were formed at >10% AR; however, the composition is unknown and may represent a mixture of the parent and TPs. Non-extractable residues were determined to be truly bound to soil given that several solvents of varying polarities were used in the extraction protocols. The majority of the applied radioactivity in the non-extractable residues was associated with the insoluble humin fraction.

(2) The 90% upper confidence bound on the mean of the five available t_R values for spiropidion in aerobic soil is 1.48 days. This value was used to calculate EECs in soil for the risk assessment.

(3) There is uncertainty in the freezer storage stability of spiropidion and SYN547305 individually. As such, degradation kinetics for the combined residue, rather than the individual compounds, was modeled.

Table 18 Estimated environmental concentrations

Substance	EEC	Method of calculation	Notes
Soil: screening level risk assessment			
Spiropidion	208 g a.i./ha	Maximum cumulative application rate to soil based on 3 × 200 g a.i./ha with a 7-day re-application interval and considering a representative half-life of 1.48 days (90% upper confidence bound on the mean of five available values) for spiropidion in aerobic soil.	EECs in g a.i./ha were used to evaluate risks to non-target terrestrial plants

Substance	EEC		Method of calculation	Notes
	0.092 mg a.i./kg dw soil		EEC of spiropidion in soil was calculated based on the maximum cumulative application rate to soil (208 g a.i./ha), and assuming a soil bulk density of 1.5 g/cm^3 and a soil depth of 15 cm.	(seedling emergence). EECs in mg/kg dw soil were used to evaluate risks to earthworms and soil-dwelling beneficial arthropods.
SYN547305	0.22 mg/kg dw soil		EECs for the major TPs in soil were calculated based on the maximum application rate (3 × 200 g a.i./ha). It was assumed that 100% of the parent transformed into each TP on a molar basis. No dissipation of the parent and TP between applications was considered. The molar conversion factor was calculated as the molecular weight of the TP divided by the molecular weight of the parent. See Appendix I, Table 16 for the molecular weight of each compound.	
SYN548033	0.23 mg/kg dw soil			
SYN552045	0.21 mg/kg dw soil			
SYN552257	0.20 mg/kg dw soil			
Water: screening level risk assessment				
Water depth:	**15 cm**	**80 cm**		
Spiropidion	236 g a.i./ha		Maximum cumulative application rate to water based on 3 × 200 g a.i./ha with a re-application interval of 7 days and considering a representative half-life of 2.60 days (maximum of two available values for spiropidion in aerobic total aquatic systems).	The EECs in surface water at 15-cm depth were used to determine risk to amphibians while the 80-cm depth EECs were used to evaluate risks to all other aquatic organisms.
	0.16 mg a.i./L	0.029 mg a.i./L	EEC of spiropidion in surface water was calculated considering a direct overspray to a one-hectare wetland with water depths of 15 and 80 cm at the above maximum cumulative application rate (236 g a.i./ha) to water.	
SYN547305	0.33 mg/L	0.062 mg/L	EECs of the major TPs in surface water were calculated based on the maximum application rate (3 × 200 g a.i./ha) assuming 100% transformation of the parent to each TP on a molar basis. No dissipation of the parent or TP between applications was considered.	
SYN548033	0.35 mg/L	0.065 mg/L		
SYN548430	0.30 mg/L	0.057 mg/L		
SYN551480	0.25 mg/L	0.046 mg/L		
SYN552045	0.32 mg/L	0.060 mg/L		
SYN552257	0.29 mg/L	0.055 mg/L		

Substance	EEC		Method of calculation	Notes
Water: refined risk assessment – spray drift (EEC in mg a.i./L) [1, 2]				
Water depth:	**15 cm**	**80 cm**		
Spiropidion	0.0094	0.0018	The screening level surface water EECs were adjusted to account for 6% spray drift deposition of medium sized spray droplets 1-metre downwind of the point of application (field sprayer).	Used in the refined risk assessment for aquatic organisms.
	0.17	0.022	The screening level surface water EECs were adjusted to account for 74% spray drift of early season airblast droplets 1-metre downwind of the point of application. This EEC is protective of spray drift from late season airblast, which results in 59% spray drift.	
Plant surfaces: Screening level and refined risk assessments				
Spiropidion	399 g a.i./ha		Maximum cumulative application rate of spiropidion to plant surfaces considering 3 × 200 g a.i./ha with a 7-day re-application interval and a default foliar half-life of 10 days.	Used to evaluate on-field and off-field risks to beneficial arthropods and non-target terrestrial plants (vegetative vigour).
	24 g a.i./ha		Off-field EEC considering 6% spray drift deposition of medium sized droplets applied by field sprayer 1-metre downwind of the point of application.	
	295 g a.i./ha		Off-field EEC considering 74% spray drift of early season airblast droplets 1-metre downwind of the point of application. This EEC is protective of spray drift from late season airblast, which results in 59% spray drift.	
Screening Level EECs for Bees (Oral exposure to pollen and/or nectar, or via direct contact)[3]				
Spiropidion	5.7 µg a.i./bee (adult)		Dose-based oral exposure estimate for bees = maximum single application rate (0.2 kg a.i./ha) × adjustment factor • Adult adjustment factor of 28.62 µg a.i./bee per kg a.i./ha was calculated as the food consumption of 0.292 g/bee per day × 98 µg a.i./g per kg a.i./ha (default tall grass residues). • Larvae adjustment factor of 12.15 µg a.i./bee per kg a.i./ha was calculated as the food consumption of 0.124 g/bee per day × 98 µg a.i./g per kg a.i./ha (default tall grass residues).	Used to evaluate risks to pollinators (bees).
	2.4 µg a.i./bee (larvae)			
	0.48 µg a.i./bee (adult)		Estimated contact exposure (µg a.i./bee) = 2.4 µg a.i./bee/1 kg a.i./ha × maximum single application rate (0.2 kg a.i./ha)	

Substance	EEC	Method of calculation	Notes
	19.6 mg a.i./kg diet	Concentration-based oral estimate for adult chronic and acute and chronic larval exposure = maximum single application rate (0.2 kg a.i./ha) × 98 µg a.i./g.	
SYN547305	4.8 µg a.i./bee (adult)	Oral exposure estimates for bees for spiropidion converted to SYN547305 on a molar basis (conversion factor of 0.83).	
	2.0 µg a.i./bee (larvae)		
	0.40 µg a.i./bee	Contact exposure estimate for bees for spiropidion converted to SYN547305 on a molar basis (conversion factor of 0.83).	
	16.3 mg a.i./kg diet	Concentration-based oral estimate for adult chronic and acute and chronic larval exposure for spiropidion, converted to SYN547305 on a molar basis (conversion factor of 0.83).	

See Appendix I, Tables 28 to 30 for the EECs in food items for birds and mammals. The EECs for birds and mammals were calculated based on 3 × 200 g a.i./ha with a 7-day re-application interval and a default foliar half-life of 10 days.

(1) Refinements for EECs in water were only required for spiropidion based on the screening level risk assessment.
(2) EECs for the runoff assessment are presented in Appendix I, Table 34.
(3) EECs for the refined risk assessment for bees are presented in Appendix I, Tables 23 and 24.

Table 19 Toxicity of spiropidion to non-target species

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
Terrestrial organisms					
Invertebrates					
Earthworm (*Eisenia fetida)*	14-d Acute	Spiropidion	LC_{50} > 1000 mg a.i./kg soil dw NOEC = 500 mg a.i./kg soil dw	A reduction in biomass at 1000 mg a.i./kg soil dw was observed.	3436806
		SYN547305	LC_{50} > 1000 mg/kg soil dw NOEC = 1000 mg/kg soil dw	No effects were observed at the highest concentration tested.	3436809
Earthworm (*Eisenia andrei*)	56-d Chronic	A20262B (301 g a.i./L)	NOEC (all endpoints) = 277 mg a.i./kg dw soil	Toxicity classification not applicable. No effects observed at the highest concentration tested.	3436811
		SYN547305	NOEC (reproduction) = 309 mg/kg dw soil	Toxicity classification not applicable. An EC_{50} (reproduction)	3436812

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
				of 936 mg/kg dw soil was determined from this study.	
		SYN548033	NOEC (reproduction) = 309 mg/kg dw soil	Toxicity classification not applicable. An EC_{50} (reproduction) of 810 mg/kg dw soil was determined from this study.	3436814
		SYN552045	NOEC (all endpoints) = 100 mg/kg dw soil	Toxicity classification not applicable. No effects observed at the highest concentration tested.	3436817
		SYN552257	NOEC (all endpoints) = 100 mg/kg dw soil	Toxicity classification not applicable. No effects observed at the highest concentration tested.	3436818
Honey bee (*Apis mellifera* L.)	48-h Contact	Spiropidion	LD_{50} > 200 µg a.i./bee	Practically non-toxic	3436778
		SYN547305	LD_{50} > 202 µg/bee	Practically non-toxic	3436781
	48-h Oral	Spiropidion	LD_{50} > 100 µg a.i./bee	Practically non-toxic	3436778
		SYN547305	LD_{50} > 101 µg/bee	Practically non-toxic	3436781
	Larval (single exposure)	Spiropidion	LD_{50} = 0.88 µg a.i./larva LC_{50} = 26 mg a.i./kg diet NOED = 0.39 µg a.i./larva	Toxicity classification not applicable	3436786
	Larval (single exposure)	SYN547305	LD_{50} = 1.00 µg/larva LC_{50} = 30 mg a.i./kg diet NOED = 0.50 µg/larva	Toxicity classification not applicable	3436789
	4-d Larval (repeated exposure)	Spiropidion	ED_{50} (adult emergence on Day 22) = 0.15 µg a.i./bee/day NOED = 0.11 µg a.i./bee/day NOEC = 2.88 mg a.i./kg diet	Toxicity classification not applicable	3436785
	4-d Larval (repeated exposure)	SYN547305	ED_{50} (adult emergence on Day 22) = 0.16 µg/bee/day NOED = 0.063 µg/bee/day	Toxicity classification not applicable	3436788

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
			NOEC = 1.58 mg a.i./kg diet		
	10-d Chronic Oral	Spiropidion	LDD_{50} = 6.8 µg a.i./bee/day NOEDD = 1.5 µg a.i./bee/day NOEC: 40 mg a.i./kg diet	There are uncertainties with this endpoint given that the concentration of the test item in the feeding solutions was not verified analytically and food consumption was not corrected for evaporation of the feeding solution.	3436777
		SYN547305	LDD_{50} = 1.4 µg/bee/day NOEDD = 0.43 µg/bee/day NOEC = 16.2 mg a.i./kg food	Toxicity classification not applicable	3436780
Bumblebee (*Bombus terrestris* L.)	48-h Contact	Spiropidion	LD_{50} > 400 µg a.i./bee NOED ≥ 400 µg a.i./bee	Practically non-toxic	3436779
	48-h Oral		LD_{50} > 198 µg a.i./bee NOED ≥ 198 µg a.i./bee	Practically non-toxic	
Predatory arthropod (*Typhlodromus pyri*)	7-d Glass plate	A20262B (301 g a.i./L)	LR_{50} > 677 g a.i./ha NOER = 677 g a.i./ha	No treatment related effects observed up to the highest concentration tested (677 g a.i./ha)	3436792
Predator, ladybird beetles	15-d Acute	Spiropidion	LR_{50} > 270 g a.i./ha NOER = 270 g a.i./ha	Toxicity classification not applicable	3436803
Predatory mite (*Hypoaspis aculeifer*)	14-d Reproduction	A20262B (301 g a.i./L)	LR_{50}/ER_{50} > 277 mg a.i./kg soil dw NOER = 277 mg a.i./kg soil dw	No effects on mortality or reproduction at the highest concentration tested	3436798
	14-d Reproduction	SYN547305	LR_{50}/ER_{50} > 1000 mg/kg soil dw NOER = 1000 mg/kg soil dw		3436800
Parasitic arthropod (*Aphidius rhopalopsiphi)*	48-h Glass plate	A20262B (301 g a.i./L)	LR_{50}/ER_{50} > 677 g a.i./ha NOER = 677 g a.i./ha	Toxicity classification not applicable	3436790

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
Parasitic wasp (*Trichogramma* sp.)	24-h Glass tube	Spiropidion	LR_{50} > 1840 g a.i./ha	Toxicity classification not applicable	3436791
Collembolan (*Folsomia candida*)	28-d Chronic	A20262B (301 g a.i./L)	NOER = 277 mg a.i./kg soil dw	Toxicity classification not applicable	3436794
	28-d Chronic	SYN547305	NOEC = 1000 mg/kg soil dw	Toxicity classification not applicable	3436796
Silkworm (*Bombyx mori*)	96-h Acute	Spiropidion	LC_{50} > 46 mg a.i./L	This study is scientifically sound but was determined to be "unacceptable for use in risk assessment" because the units cannot be converted for use in the risk assessment. No adverse effects were observed in the study.	3436805
Birds					
Bobwhite quail (*Colinus virginianus*)	Acute oral	Spiropidion	LD_{50} = 959 mg a.i./kg bw	Slightly toxic	3436714
	5-d Dietary	Spiropidion	LC_{50} > 5620 ppm a.i. LD_{50} >1049 mg a.i./kg bw/d	Practically non-toxic. 20% mortality occurred at the highest dose tested	3436717
	One-generation (22-week) reproductive toxicity	Spiropidion	NOED = 38.8 mg a.i./kg bw/d LOED > 38.8 mg a.i./kg bw/d	Toxicity classification not applicable	3436719
Mallard duck (*Anas platyrhynchos*)	Acute oral	Spiropidion	$LD_{50} \geq$ 957 mg a.i./kg bw	Regurgitation occurred in all birds given a dose of ≥1014 mg a.i./kg bw. No regurgitation was observed in birds given doses of ≤ 904 mg a.i./kg bw. The LD_{50} value was estimated by nonlinear interpolation to be equal to, or greater than, the	4346715

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
				50% regurgitation level (≥957 mg a.i./kg bw).	
	5-d Dietary	Spiropidion	LC_{50} > 5620 ppm a.i. LD_{50} >1413 mg a.i./kg bw/d	Practically non-toxic. 20% mortality occurred in the 5620 ppm a.i. treatment.	4346716
	One-generation (23-week) reproductive toxicity	Spiropidion	NOED = 20 mg a.i./kg bw/d LOED = 60 mg a.i./kg bw/d	Toxicity classification not applicable	3436720
Zebra finch (*Taeniopygenia guttata*)	5-d Dietary	Spiropidion	LC_{50} = 509 ppm a.i.	Moderately toxic. Food avoidance was observed in the three highest treatments (150, 300 and 600 ppm). An LD_{50} was not be calculated due to food avoidance in the 600 ppm a.i treatment resulting in a non-monotonic dose response. 60% mortality occurred in the 600 ppm a.i. treatment.	3436718
Mammals					
Rat	Acute oral	Spiropidion	LD_{50} > 2000 mg a.i./kg bw	Practically non-toxic	3161304
	Two generational reproduction		NOAEL = 24 mg a.i./kg bw LOAEL > 24 mg a.i./kg bw	Toxicity classification not applicable. No adverse effects on reproduction observed up to the highest concentration tested.	3161339
Vascular plants					
Non-target terrestrial plants	Seedling emergence (all species)	A20262B (301 g a.i./L)	ER_{25} > 603 g a.i./ha NOER = 603 g a.i./ha	No treatment related effects noted up to the highest concentration tested (603 g a.i./ha)	3436729

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
	Vegetative vigour (maize, dry weight)	+ Citrol-ina (paraffin oil)	ER_{50} = 307 g a.i./ha NOER = 66.2 g a.i./ha	Toxicity classification not applicable	3436728
Freshwater organisms					
Daphnia magna	48-h Acute (static)	Spiropidion	EC_{50} = 9.0 mg a.i./L NOEC = 4.4 mg a.i./L	Moderately toxic	3436754
		SYN547305	EC_{50} > 103 mg/L NOEC = 103 mg/L	Practically non-toxic	3436755
	21-d Chronic (flow-through)	Spiropidion	NOEC (reproduction) = 0.32 mg a.i./L	Toxicity classification not applicable. The most sensitive endpoint is based on a reduction in reproduction.	3436766
Midge (*Chironomus riparius*)	48-h Acute (water exposure; static-renewal)	Spiropidion	EC_{50} = 0.61 mg a.i./L NOEC = 0.52 mg a.i./L	Highly toxic	3436756
		SYN547305	EC_{50} > 7.1 mg/L NOEC = 3.7 mg/L	40% cumulative mortality was observed at the highest concentration tested (7.1 mg/L)	3436757
		SYN548033	EC_{50} = 17 mg/L NOEC = 13 mg/L	Slightly toxic	3436758
	48-h Acute (water exposure; static)	SYN548274	EC_{50} > 101 mg/L NOEC = 46 mg/L	Practically non-toxic	3436759
		SYN548430	EC_{50} > 93 mg/L NOEC = 42 mg/L	45% immobilized larvae were observed after 48 hours at the highest concentration tested (93 mg/L).	3436760
		SYN551480	EC_{50} > 94 mg/L NOEC = 94 mg/L	Practically non-toxic	3436763
		SYN552045	EC_{50} = 37 mg/L NOEC = 20 mg/L	Slightly toxic	3436764

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
		SYN552257	EC_{50} >89 mg/L NOEC = 41 mg/L	Immobilization of 35% of the larvae was observed after 48 hours at the highest concentration tested (89 mg/L)	3436765
Amphipod *(Hyalella azteca)*	10-d Sediment (flow-through)	Spiropidion	**Initial measured sediment concentration** LC_{50} > 33 mg a.i./kg NOEC = 12 mg a.i./kg **Geometric mean measured pore water concentration** LC_{50} > 0.93 mg a.i./L NOEC = 0.30 mg a.i..L	The most sensitive endpoint based on the pore water concentration used in the risk assessment.	3436773
Midge *(Chironomus dilutus)*	10-d Sediment (flow-through)	Spiropidion	**Initial measured sediment concentration** LC_{50} > 13 mg a.i./kg NOEC = 1.6 mg a.i./kg **Geometric mean measured pore water concentration** LC_{50} > 0.31 mg a.i./L NOEC = 0.02 mg a.i./L	The most sensitive endpoint based on the pore water concentration used in the risk assessment.	3436775
Rainbow trout (*Oncorhynchus mykiss*)	96-h Acute (flow-through)	Spiropidion	LC_{50} = 0.56 mg a.i./L NOEC = 0.39 mg a.i./L	Highly toxic	3436744
	96-h Acute (static conditions)	SYN547305	LC_{50} >76 mg/L NOEC = 76 mg/L	Practically non-toxic up to the highest concentration tested (76 mg/L)	3436746
Common carp (*Cyprinus carpio*)	96-h Acute (flow-through)	Spiropidion	LC_{50} = 1.0 mg a.i./L NOEC = 0.33 mg a.i./L	Highly toxic	3436748
Fathead minnow (*Pimephales promelas*)	96-h Acute (flow-through)	Spiropidion	LC_{50} = 2.6 mg a.i./L NOEC = 1.7 mg a.i./L	Moderately toxic	3436750

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
Fathead minnow (*Pimephales promelas*)	33-d Early life stage (flow-through)	Spiropidion	NOEC = 0.11 mg a.i./L	Toxicity classification not applicable. The most sensitive endpoint is based on reduced length and dry weight.	3436752
Amphibians	96-h Acute (rainbow trout surrogate; flow-through)	Spiropidion	LC_{50} = 0.56 mg a.i./L	Highly toxic	3436744
		SYN547305	LC_{50} > 76 mg/L	Moderately toxic	3436750
	Chronic (fathead minnow surrogate; flow-through)	Spiropidion	NOEC = 0.11 mg a.i./L	Toxicity classification not applicable	3436752
Freshwater algae (*Anabaena flos-aquae)*	96-h Acute (static)	Spiropidion	EC_{50} > 14 mg a.i./L NOEC = 14 mg a.i./L	Practically non-toxic up to the highest concentration tested	3436767
Freshwater diatom (*Navicula pelliculosa)*	96-h Acute (static)	Spiropidion	EC_{50} = 1.4 mg a.i./L NOEC = 0.084 mg a.i./L	Moderately toxic. The most sensitive endpoint is based on a inhibition in area under the growth curve and yield.	3436768
Freshwater algae (*Rhaphidocelis subcapitata*)	96-h Acute (static)	Spiropidion	72-h EC_{50} = 4.1 mg a.i./L 96-h NOEC = 0.78 mg a.i./L	Moderately toxic. The 72-h EC_{50} value for area under the curve was more sensitive than the 96-h EC_{50} and was used in the risk assessment.	3436769
	96-h Acute (static)	SYN547305	72-h EC_{50} = 27 mg/L 72-h/96-h NOEC = 20 mg/L	Slightly toxic. The 72-h EC_{50} value for yield was more sensitive than the 96-h endpoints and was used in the risk assessment.	3436771

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[(1)] and/or comments	PMRA No.
Vascular plants (*Lemna gibba*)	7-day (static-renewal)	Spiropidion	EC_{50} = 1.4 mg a.i./L NOEC = 0.22 mg a.i./L	Moderately toxic. The most sensitive endpoint is based on a inhibition in yield (frond number).	3436776
Marine organisms					
Saltwater mysid (*Americamysis bahia*)	96-h Acute (flow-through)	Spiropidion	LC_{50} = 2.9 mg a.i./L NOEC = 2.0 mg a.i./L	Moderately toxic	3436724
	28-day Chronic (flow-through)	Spiropidion	NOEC = 0.015 mg a.i./L	Toxicity classification not applicable. The most sensitive endpoint is based on a reduction in female dry weight.	3436726
Eastern oyster (*Crassostrea virginica*)	96-h Acute (flow-through)	Spiropidion	EC_{50} = 0.32 mg a.i./L NOEC = 0.17 mg a.i./L	No mortality was observed up to the highest concentration tested (1.4 mg a.i./L). The most sensitive endpoint is based on reduced shell growth.	3436723
Amphipod (*Leptocheirus plumulosus*)	10-d Sediment (flow-through)	Spiropidion	**Initial measured sediment concentration** LC_{50} > 40 mg a.i./kg NOEC = 40 mg a.i./kg **Geometric mean pore water concentration** LC_{50} > 0.45 mg a.i./L NOEC = 0.45 mg a.i./L	No effects were observed at the highest treatment tested. The most sensitive endpoint based on the pore water concentration was used in the risk assessment.	3436774
Sheepshead minnow (*Cyprinodon variegatus*)	96-h Acute (flow-through conditions)	Spiropidion	LC_{50} = 1.2 mg a.i./L NOEC = 0.37 mg a.i./L	Moderately toxic	3436725
	34-d Early life stage (flow-through conditions)	Spiropidion	NOEC = 0.025 mg a.i./L	Toxicity classification not applicable. The most sensitive endpoint was based on a reduction in hatching success and overall survival..	3436727

Organism	Exposure	Test substance	Endpoint	Degree of toxicity if applicable[1] and/or comments	PMRA No.
Marine diatom (*Skeletonema costatum*)	96-h Acute	Spiropidion	72-h EC_{50} = 0.39 mg a.i./L 96-h NOEC = 0.11 mg a.i./L	Highly toxic. The 72-h EC_{50} for yield was more sensitive than the 96-h values and was used in the risk assessment.	3436770

Spiropidion = SYN46330
(1) US EPA classification for acute toxicity, where applicable

Table 20 Screening level risk assessment for non-target terrestrial species (Excluding birds and mammals)

Test organism	Exposure	Test substance	EEC	Endpoint value	UF	Effects metric	RQ[1]	LOC	LOC exceeded?
Terrestrial organisms									
Invertebrates									
Earthworm (*Eisenia fetida)*	14-d Acute	Spiropidion	0.092 mg a.i./kg dw soil	> 1000 mg a.i./kg dw soil	2	> 500 mg a.i./kg dw soil	< 0.0002	1	No
		SYN547305	0.22 mg/kg dw soil	> 1000 mg/kg dw soil	2	> 500 mg/kg dw soil	< 0.0004	1	No
Earthworm (*Eisenia andrei*)	56-d Chronic	A20262B (301 g a.i./L)	0.092 mg a.i./kg dw soil	277 mg a.i./kg dw soil	1	277 mg a.i./kg dw soil	0.0003	1	No
		SYN547305	0.22 mg/kg dw soil	309 mg/kg dw soil	1	309 mg/kg dw soil	0.0007	1	No
		SYN548033	0.23 mg/kg dw soil	309 mg/kg dw soil	1	309 mg/kg dw soil	0.0007	1	No
		SYN552045	0.21 mg/kg dw soil	100 mg/kg dw soil	1	100 mg/kg dw soil	0.0021	1	No
		SYN552257	0.20 mg/kg dw soil	100 mg/kg dw soil	1	100 mg/kg dw soil	0.0020	1	No
Honey bee (*Apis mellifera* L.)	48-h Contact	Spiropidion	0.48 µg a.i./bee	> 200 µg a.i./bee	1	> 200 µg a.i./bee	<0.0024	0.4	No
		SYN547305	0.40 µg/bee	> 202 µg/bee	1	> 202 µg/bee	<0.0020	0.4	No
	48-h Oral	Spiropidion	5.7 µg a.i./bee	> 100 µg a.i./bee	1	> 100 µg a.i./bee	<0.057	0.4	No

Test organism	Exposure	Test substance	EEC	Endpoint value	UF	Effects metric	RQ[(1)]	LOC	LOC exceeded?
		SYN547305	4.7 µg/bee	> 101 µg/bee	1	> 101 µg/bee	<0.047	0.4	No
	Larval (single exposure)	Spiropidion	2.4 µg a.i./larva	0.88 µg a.i./larva	1	0.88 µg a.i./larva	**2.8**	0.4	**Yes**
			19.6 mg a.i./kg diet	26 mg a.i./kg diet	1	26 mg a.i./kg diet	0.75	0.4	No
	Larval (single exposure)	SYN547305	2.0 µg/larva	1.0 µg/larva	1	1.0 µg/larva	**2.0**	0.4	**Yes**
			16.3 mg a.i./kg diet	30 mg a.i./kg diet	1	30 mg a.i./kg diet	0.54	0.4	No
	4-d Larval (repeated exposure)	Spiropidion	2.4 µg a.i./bee/d	0.11 µg a.i./bee/d	1	0.11 µg a.i./bee/d	**21**	1	**Yes**
			19.6 mg a.i./kg diet	2.88 mg a.i./kg diet	1	2.88 mg a.i./kg diet	**6.8**	1	**Yes**
	4-d Larval (repeated exposure)	SYN547305	2.0 µg/bee/d	0.063 µg/bee/d	1	0.063 µg/bee/d	**32**	1	**Yes**
			16.3 mg a.i./kg diet	1.58 mg a.i./kg diet	1	1.58 mg a.i./kg diet	**10**	1	**Yes**
	10-d Adult Chronic Oral	Spiropidion	5.7 µg a.i./bee/d	1.5 µg a.i./bee/d	1	1.5 µg a.i./bee/d	**3.8**	1	**Yes**
			19.6 mg a.i./kg diet	40 mg a.i./kg diet	1	40 mg a.i./kg diet	0.49	**1**	No
		SYN547305	4.7 µg/bee/d	0.43 µg/bee/d	1	0.43 µg/bee/d	**11**	1	**Yes**
			16.3 mg a.i./kg diet	16.2 mg a.i./kg food	1	16.2 mg a.i./kg food	**1**	1	**Yes**
Bumblebee (*Bombus terrestris* L.)	48-h Contact	Spiropidion	0.48 µg a.i./bee	> 400 µg a.i./bee	1	> 400 µg a.i./bee	<0.0012	0.4	No
	48-h Oral		5.7 µg a.i./bee	> 198 µg a.i./bee	1	> 198 µg a.i./bee	<0.029	0.4	No
Predatory arthropod (*Typhlodromus pyri*)	7-d Glass plate	A20262B (301 g a.i./L)	399 g a.i./ha	> 677 g a.i./ha	1	> 677 g a.i./ha	<0.59	2	No

Test organism	Exposure	Test substance	EEC	Endpoint value	UF	Effects metric	RQ[(1)]	LOC	LOC exceeded?
Predator, ladybird beetles	15-d Acute	Spiropidion	399 g a.i./ha	> 270 g a.i./ha	1	> 270 g a.i./ha	**< 1.5**	1	**Yes**
Predatory mite (*Hypoaspis aculeifer*)	14-d Reproduction	A20262B (301 g a.i./L)	0.092 mg a.i./kg dw soil	> 277 mg a.i./kg dw soil	1	> 277 mg a.i./kg dw soil	< 0.0003	1	No
	14-d Reproduction	SYN547305	0.077 mg a.i./kg dw soil	> 1000 mg a.i./kg dw soil	1	> 1000 mg a.i./kg dw soil	< 0.0001	1	No
Parasitic arthropod (*Aphidius rhopalopsiphi*)	48-h Glass plate	A20262B (301 g a.i./L)	399 g a.i./ha	> 677 g a.i./ha	1	> 677 g a.i./ha	<0.59	2	No
Parasitic wasp (*Trichogramma* sp.)	24-h Glass tube	Spiropidion	399 g a.i./ha	> 1840 g a.i./ha	1	> 1840 g a.i./ha	<0.22	1	No
Collembolan (*Folsomia candida*)	28-d Chronic	A20262B (301 g a.i./L)	0.092 mg a.i./kg dw soil	277 mg a.i./kg dw soil	1	277 mg a.i./kg dw soil	0.0003	1	No
	28-d Chronic	SYN547305	0.077 mg a.i./kg dw soil	1000 mg a.i./kg dw soil	1	1000 mg a.i./kg dw soil	0.0001	1	No
Vascular plants									
Non-target terrestrial plants	Seedling emergence (all species)	A20262B (301 g a.i./L) + Citrol-ina (parrafin oil)	208 g a.i./ha	> 603 g a.i./ha	1	> 603 g a.i./ha	< 0.34	1	No
	Vegetative vigour (maize,		399 g a.i./ha	307 g a.i./ha	2	154 g a.i./ha	**2.6**	1	**Yes**

Test organism	Exposure	Test substance	EEC	Endpoint value	UF	Effects metric	RQ[1]	LOC	LOC exceeded?
	dry weight)								

Bold: RQ exceeds LOC

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 21 Refined risk assessment for beneficial arthropods and non-target terrestrial plants

Organism	Exposure	Test substance	EEC (g a.i./ha)	Endpoint (g a.i./ha)	UF	Effects metric (g a.i./ha)	RQ[1]	LOC	LOC exceeded?
6% Spray drift (field sprayer, medium spray)									
Invertebrates									
Predator, ladybird beetles	15-d Acute	Spiropidion	24	>270	1	270	<0.0887	1	No
Vascular plants									
Non-target terrestrial plants	Vegetative vigour (maize, dry weight)	A20262B (301 g a.i./L) + Citrol-ina (parrafin oil)	24	307	2	154	0.2	1	No
74% Spray drift (early airblast)									
Invertebrates									
Predator, ladybird beetles	15-d Acute	Spiropidion (SYN46330)	295	>270	1	270	**<1.1**	1	**Yes**

Organism	Exposure	Test substance	EEC (g a.i./ha)	Endpoint (g a.i./ha)	UF	Effects metric (g a.i./ha)	RQ(1)	LOC	LOC exceeded?
Vascular plants									
Non-target terrestrial plants	Vegetative vigour (maize, dry weight)	A20262B (301 g a.i./L) + Citrol-ina (parrafin oil)	295	307	2	154	**1.9**	1	**Yes**

Bold: RQ exceeds LOC

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 22 Residues of Spiropidion and SYN547305 in pollen and nectar from sprayed field crops

PMRA No.	Crop	Use pattern	Trial location(s)(1)	Sampling interval with max. concentrations	Spiropidion				SYN547305			
					Nectar (ppb)		Pollen (ppb)		Nectar (ppb)		Pollen (ppb)	
					Max.	Mean	Max.	Mean	Max.	Mean	Max.	Mean
3494921	Cucumber	3 × 180 g a.i./ha, 7-d interval, applied 19, 12 and 5 days prior to bloom	USA: **North Carolina**, Missouri and California	7 ± 1 DA3A	0.25	0.25	12.4	11.5	141	74.5	1730	1570
	Cucumber	3 × 180 g a.i./ha, 7-d interval. 1st application was made prior to bloom, with the remaining two during bloom.		0 DA3A	1.29	1.06	46 740	19 166	804	711	52 530	28 549
3436734	Dry Bean(2)	3 × 120 g a.i./ha, 7-d interval. 1st application was made at early bloom. Bloom was	Brazil: **Itápolis** and Ponta Grossa	1 DAA2	55.8	54.2	50.9	20.9	2060	1090	166	80.2

PMRA No.	Crop	Use pattern	Trial location(s)[1]	Sampling interval with max. concentrations	Spiropidion				SYN547305			
					Nectar (ppb)		Pollen (ppb)		Nectar (ppb)		Pollen (ppb)	
					Max.	Mean	Max.	Mean	Max.	Mean	Max.	Mean
		ending when last application was applied.										
		3 × 120 g a.i./ha, 7-d interval. 1st application 10 days after emergence, 2nd at early bloom and the 3rd at full bloom.		1 DAA3	34.4	32.1	96.3	50.7	1920	1740	306	184
		3 × 75 g a.i./ha, 7-d interval. 1st application at early bloom. Bloom was ending when last application was applied.		1 DAA2	94.7	58.4	75	57.2	1630	1517	97.8	77.5
3436736	Cucumber	2 × 160 g a.i./ha, 7-d interval. Final application just before bloom.	France, Germany, Spain, **Italy**	14 DAA2 (earliest opportunity)	5[3]	N/A[4]	160	N/A[4]	710	N/A[4]	2800	N/A[4]
		3 × 160 g a.i./ha, 6 to 7-d interval. All three applications during bloom.		1 DAA3	5[3]	N/A[4]	200	N/A[4]	8700	N/A[4]	22000	N/A[4]
3436737	Apple	2 × 300 g a.i./ha, 7-day interval. 1st application before bloom, 2nd at early bloom (10% bloom)	United States (**New York**, Washington) and Canada (Quebec)	1-2 DAA2	51.7	35.4	452 715	319 422	1733	1300	76 623	67 600

PMRA No.	Crop	Use pattern	Trial location(s)[1]	Sampling interval with max. concentrations	Spiropidion				SYN547305			
					Nectar (ppb)		Pollen (ppb)		Nectar (ppb)		Pollen (ppb)	
					Max.	Mean	Max.	Mean	Max.	Mean	Max.	Mean
3436739	Tomato	4 × 120 g a.i./ha, 7-day interval. All applications during bloom.	Brazil: **Mogi Guaçú, São Paulo** and Catalão, Goiás	1 DAA3	No value[5]		2330	1517	No value[5]		36000	31400
		3 × 60 g a.i./ha, 7-day interval. All applications during bloom. Test item was a co-formulation with acetamiprid.		1 DAA1			6240	4090			5407	3100
3436782	*Phacelia tanacetifolia* (semi-field tunnel study)	2 × 300 g a.i./ha. 1st application was at early bloom, with the 2nd 8 days later during full bloom.	**Germany**	1 DAA2	40	N/A [4]	900	N/A	1000	N/A [4]	4600	N/A[4]
3524458	Sunflower (*Helianthus annuus*; semi-field tunnel study)	3 × 180 g a.i./ha, 7-day interval. 1st application before bloom with the last two were during bloom.	**Brazil**	4 DAA3	3	N/A [4]	558	N/A	5	N/A [4]	7810	N/A[4]

(1) The pollen and nectar concentrations from the sampling interval that resulted in the highest EEC is reported for each trial; the site with the highest EECs is shown in **bold.** EECs for adult and larval bees are presented in Appendix I, Tables 23 and 24.
(2) Residues in anthers were used as a surrogate for pollen.
(3) Value less than the limit of quantification (LOQ). The value was replaced by 0.5 × LOQ.
(4) N/A - data not available to calculate mean values.
(5) No value because tomato plants do not produce nectar

Table 23 Refined screening level (Tier I) RQs for bees (on a µg/bee Basis) using residue data from field crops

Crop	Use pattern	Adult oral EECs (µg/bee/d in SYN547305 equivalents)[1, 2]		Larval oral EECs (µg/bee/d in SYN547305 equivalents)[1, 2]		RQs based on:		
		Based on max. residue[3]	Based on mean residue[4]	Based on max. residue[3]	Based on mean residue[4]	Larval (single exposure): LD_{50} = 1.00 µg/larva (LOC = 0.4)	4-d Larval (repeat exposure): NOED = 0.063 µg/bee/day (LOC = 1)	10-d Chronic Oral (adult): NOEDD = 0.43 µg/bee/day (LOC = 1)
Cucumber	3 × 180 g a.i./ha, 7-d interval, applied 19, 12 and 5 days prior to bloom	0.04	0.02	0.02	0.01	0.02	0.23	0.05
	3 × 180 g a.i./ha, 7-d interval. 1st application was made prior to bloom, with the remaining two during bloom.	0.24	0.21	0.49	0.27	**0.49**	**4.3**	0.49
Dry Bean	3 × 120 g a.i./ha, 7-d interval. 1st application was made at early bloom. Bloom was ending when last application was applied.	0.62	0.34	0.26	0.14	0.26	**2.2**	0.78
	3 × 120 g a.i./ha, 7-d interval. 1st application 10 days after emergence, 2nd at early bloom and the 3rd at full bloom.	0.57	0.52	0.24	0.21	0.24	**3.4**	**1.2**
	3 × 75 g a.i./ha, 7-d interval. 1st application at early bloom. Bloom was ending when last application was applied.	0.51	0.46	0.21	0.19	0.21	**3.0**	**1.1**
Cucumber	2 × 160 g a.i./ha, 7-d interval. Final application just before bloom.	0.21	0.00	0.10	0.00	0.10	**1.5**[5]	0.49[5]

Crop	Use pattern	Adult oral EECs (µg/bee/d in SYN547305 equivalents)[1, 2]		Larval oral EECs (µg/bee/d in SYN547305 equivalents)[1, 2]		RQs based on:		
		Based on max. residue[3]	Based on mean residue[4]	Based on max. residue[3]	Based on mean residue[4]	Larval (single exposure): LD_{50} = 1.00 µg/larva (LOC = 0.4)	4-d Larval (repeat exposure): NOED = 0.063 µg/bee/day (LOC = 1)	10-d Chronic Oral (adult): NOEDD = 0.43 µg/bee/day (LOC = 1)
	3 × 160 g a.i./ha, 6 to 7-d interval. All three applications during bloom.	2.54	0.00	1.12	0.00	**1.1**	**18**[5]	**5.91**[5]
Apple	2 × 300 g a.i./ha, 7-day interval. 1st application before bloom, 2nd at early bloom (10% bloom)	0.55	0.41	2.46	1.80	**2.5**	**29**	0.96
Tomato[6]	4 × 120 g a.i./ha, 7-day interval. All applications during bloom.	0.0016	0.0014	0.14	0.13	0.14	**2.0**	0.003
	3 × 60 g a.i./ha, 7-day interval. All applications during bloom. Test item was a co-formulation with acetamiprid.	0.0015	0.0011	0.13	0.10	0.13	**1.6**	0.003

RQs that exceed the LOC are **bolded**

(1) The pollen and nectar concentrations from the sampling interval that resulted in the highest EEC for each trial was used in the risk assessment.

(2) EECs were calculated according to the Guidance for Assessing Pesticide Risks to Bees:
Consumptions rates for adults (mg/day): 0 for royal jelly, 292 for nectar and 0.041 for pollen
Consumptions rates for larvae (mg/day): 0 for royal jelly, 120 for nectar and 3.6 for pollen
Data for royal jelly not available; however, this does not affect the EEC calculation as the consumption rate for royal jelly in the pollinator guidance is 0. As such, it was excluded from the EEC equations.

(3) Maximum residues used to estimate acute exposure.

(4) Mean residues used to estimate chronic exposure.

(5) Maximum EECs were used to estimate chronic risk because mean values are not available.

(6) Tomatoes do not produce nectar. As such, the EECs were calculated with the nectar contribution equal to zero.

Table 24 Refined screening level (Tier I) RQs for bees (mg/kg diet basis) using residue data from field crops

Crop	Use pattern	EECs (mg/kg diet in SYN547305 equivalents)[1, 2]			RQs based on:		
		Adult based on mean residue [4]	Larvae based on mean residue [4]	Larvae based on max residue [3]	Larval (single exposure): LC_{50} = 30 mg/kg diet (LOC = 0.4)	4-d Larval (repeat exposure): NOEC = 1.58 mg/kg diet (LOC = 1)	10-d Chronic Oral (adult): NOEC = 16.2 mg/kg diet (LOC = 1)
Cucumber[5]	3 × 180 g a.i./ha, 7-d interval, applied 19, 12 and 5 days prior to bloom	0.075	0.12	0.19	0.01	0.08	0.005
	3 × 180 g a.i./ha, 7-d interval. 1st application was made prior to bloom, with the remaining two during bloom.	0.72	2.20	3.90	0.13	**1.4**	0.04
Dry Bean	3 × 120 g a.i./ha, 7-d interval. 1st application was made at early bloom. Bloom was ending when last application was applied.	1.16	1.13	2.07	0.07	0.71	0.07
	3 × 120 g a.i./ha, 7-d interval. 1st application 10 days after emergence, 2nd at early bloom and the 3rd at full bloom.	1.78	1.73	1.92	0.06	**1.1**	0.11
	3 × 75 g a.i./ha, 7-d interval. 1st application at early bloom. Bloom was ending when last application was applied.	1.59	1.55	1.70	0.06	0.98	0.10
Cucumber[5]	2 × 160 g a.i./ha, 7-d interval. Final application just before bloom.	0.72 (max)	0.78 (max)	0.78	0.03	0.50	0.04

Crop	Use pattern	EECs (mg/kg diet in SYN547305 equivalents)[1, 2]			RQs based on:		
		Adult based on mean residue [4]	Larvae based on mean residue [4]	Larvae based on max residue [3]	Larval (single exposure): LC_{50} = 30 mg/kg diet (LOC = 0.4)	4-d Larval (repeat exposure): NOEC = 1.58 mg/kg diet (LOC = 1)	10-d Chronic Oral (adult): NOEC = 16.2 mg/kg diet (LOC = 1)
	3 × 160 g a.i./ha, 6 to 7-d interval. All three applications during bloom.	8.70 (max)	9.10 (max)	9.10	0.30	**5.8**	0.54
Apple	2 × 300 g a.i./ha, 7-day interval. 1st application before bloom, 2nd at early bloom (10% bloom)	1.41	14.5	19.9	**0.66**	**9.2**	0.09
Tomato	4 × 120 g a.i./ha, 7-day interval. All applications during bloom.	0.005	1.02	1.15	0.04	0.65	0.003
	3 × 60 g a.i./ha, 7-day interval. All applications during bloom. Test item was a co-formulation with acetamiprid.	0.004	0.82	1.04	0.03	0.52	0.002

RQs that exceed the LOC are **bolded**

(1) The pollen and nectar concentrations from the sampling interval that resulted in the highest EEC for each trial was used in the risk assessment.

(2) EECs were calculated as follows:

Consumptions rates for foraging bees (mg/kg diet):

Measured concentration in nectar (mg/kg) × 292/(292 + 0.041) + measured concentration in pollen (mg/kg) × 0.041/(292 + 0.041)

Consumptions rates for larvae (mg/kg diet):

Measured concentration in nectar (mg/kg) × 120/(120 + 3.6) + measured concentration in pollen (mg/kg) × 3.6/(120 + 3.6)

(3) Maximum residues used to estimate acute exposure.

(4) Mean residues used to estimate chronic exposure.

(5) Maximum EECs were used to estimate chronic risk because mean values are not available.

Table 25 Summary of Tier II studies for pollinators

Study design	Summary and conclusions	PMRA No.
Study type: Semi-field study (Tier II) in Germany **Test species:** *Apis mellifera* L. **Crop:** *Phacelia tanacetifolia* **Test item:** A20262B (300 g a.i./L) **Application rate and timing:** 2 × 300 g a.i./ha tank mixed with 0.25% v/v the adjuvant, A20647A (5% acetic acid ethynyl ester, polymer with ethenol) First application at the early bloom with the second application 8 days later at full bloom. **Tunnel size:** 100 m^2 with 83.7 m^2 of crop **Mean colony size before exposure:** Control: 9214 ± 1207 bees Treatment: 8011 ± 1222 bees Reference toxicant: 8385 ± 2800 bees **Test duration:** 75 days total Pre-exposure:1 day Exposure: 7 days Pots-observation period: 58 days **Number of replicates:** Four tunnels/treatment	Two applications of the formulated product, A20262B, were applied to flowering *Phacelia tanacetifolia* at a rate of 300 g a.i./ha each. Commercial bee colonies were placed in tunnels the evening before the second application. A water control and a reference toxicant (300 g fenoxycarb/ha) were applied the same day as the second application of A20262B. Bees were in flight during the second application. The mortality and behaviour of the bees and the condition of the colonies were examined before and after application. Foraging activity was observed during the exposure phase in the tunnels. The condition of the colonies and the brood development of previously marked eggs, young larvae and old larvae were checked regularly after set-up in the tunnels. Samples of forager bees (for preparation of pollen and nectar samples), leaves, flowers and samples of soil were collected during the exposure phase and analyzed for residues of spiropidion and SYN547305. Overall, there were no spiropidion-related effects on adult worker bee mortality, pupal mortality, foraging activity or behaviour, brood and compensation indices or brood termination when compared to the control. The spiropidion treatment colony strength was similar to the controls. Exposure to fenoxycarb, the reference toxicant, resulted in decreased brood development, and increased brood termination and pupal mortality when compared to the controls. No residues of spiropidion or SYN547305 were measured above the limit of quantification in samples from the control tunnels. Maximum residues of spiropidion in pollen, nectar, leaf and flower samples collected up to 7 days after the second application were 0.90, 0.04, 32 and 34 mg/kg, respectively, while the SYN547305 concentrations were 4.6, 1.0, 23 and 14 mg/kg. Due to the rapid transformation of spiropidion, the total residues of	3436782

Study design	Summary and conclusions	PMRA No.
	spiropidion and SYN547305 should be considered in matrices other than pollen rather than spiropidion alone. **Considerations**: The single application rate (300 g a.i./ha) is higher than the maximum single application rate proposed for Canada (200 g a.i./ha). The cumulative rate (600 g a.i./ha) is consistent with proposed. Residues in the plant matrices confirm exposure to spiropidion and SYN547305.	
Study type: Semi-field study (Tier II) in Brazil **Test species:** *Apis mellifera* L. **Crop:** sunflower (*Helianthus annus*) **Test item:** A20262B (303 g a.i./L) **Application rate and timing:** 3 × 180 g a.i./ha tank mixed with 0.25% v/v the adjuvant, Assist (75.6% mineral oil), with a 7-day interval. First application before bloom of sunflowers (BBCH 59), second and third applications were during bloom (BBCH 61-69). **Tunnel size:** Effect tunnels: 150 m^2 Residue tunnels: 240 m^2 **Mean colony size before exposure:** Control: 7615 bees Treatment: 7561 bees Reference toxicant: 7633 bees **Test duration:** 49 days total Pre-exposure: 3 days Exposure: 7 days Post-observation period at the monitoring site: 39 days **Number of replicates:** Five tunnels/treatment (4 replicates to determine effects, one tunnel to determine residues).	Three applications of the formulated product, A20262B, were applied to sunflowers at a rate of 180 g a.i./ha, tank mixed with 0.25% v/v of the adjuvant, Assist (mineral oil). Commercial bee colonies were installed in the tunnels in the evening three days before the 3rd application. A water control and a reference toxicant (dimethoate) were also applied the same day as the third application of A20262B. Bees were in flight for the 3rd application. Bees were maintained in the tunnels until 7 days after the third application of the test item. Mortality and behaviour were assessed daily for a period of 4 days before, and for 46 days after, the test item application. The conditions of the colonies and bee brood development were assessed twice before the test item application and eight times until 45 days after the test item application. The flight activity was assessed daily for a period of 7 days during the tunnel phase. Samples of soil, pollen and nectar (from forager bees), leaves and flowers were collected from two separate tunnel tents (C101-05 and T102-05) during the study for analysis of spiropidion and SYN547305 residues. No unusual behaviour of the honeybees was observed. The test item did not result in significant effects on worker bee mortality or colony condition (number of bees, number of brood cells or number of food cells) compared to the control; however, it did result in a reduction of flight activity on the day of application. The bees appeared to have recovered from this effect by 1 day	3436783

Study design	Summary and conclusions	PMRA No.
	after application 3 (1 DAA3). The study did not calculate brood termination rate, brood index or compensation index. Exposure to dimethoate resulted in reduced flight activity on the day of application, increased adult bee mortality and a decrease in the number of pollen cells compared to the control group. No residues of spiropidion or SYN547305 above the limit of quantification were measured in samples from the control tunnels. Residues of spiropidion and SYN547305 were found in treated leaf, flowers, pollen and nectar samples collected up to 7 DAA3. The concentrations of spiropidion and SYN547305 were generally highest on the day of the application and decreased over the course of the following seven days. Exceptions to this were the pollen samples collected after the 3rd application; the 4 DAA3 samples had the highest levels for both analytes. The maximum residues of spiropidion in pollen and nectar were 558 ppb (4 DAA3) and 6 ppb (1 DAA3), respectively. The maximum residues of SYN547305 in pollen and nectar were 7810 ppb (4 DAA3) and 5 ppb (1 and 4 DAA3), respectively. Due to the rapid transformation of spiropidion, the total residues of spiropidion and SYN547305 should be considered rather than spiropidion alone. **Considerations**: The single and cumulative application rates used in this study are lower than the maximum single and cumulative application rates proposed for Canada (3 × 180 g a.i./ha vs. 3 × 200 g a.i./ha). Residues in the plant matrices confirm exposure to spiropidion and SYN547305.	
Study type: Colony feeding study (Tier II) in Germany; in-hive feeding method **Test species:** *Apis mellifera* L.	A study to evaluate the effects of an oral exposure of spiropidion (98.4% purity) on honeybee colonies was conducted. Free-foraging honeybee colonies were provided with one litre of untreated or treated sucrose with 2% acetone solution for a period of approximately 40 to 71 hours. Mortality, behaviour of bees, brood development and	3436784

Study design	Summary and conclusions	PMRA No.
Crop: N/A – test item was applied in-hive at a site with access to natural nectar and pollen sources. **Test item:** Spiropidion (98.4% purity) **Application rate and method:** 1 untreated control, 4 dose rates of the test item (4.71, 9.41, 18.83 and 37.66 ppm) and one dose rate of the reference item (0.75 g fenoxycarb/L). The application was performed with an in-hive feeding method by providing 1 L treated/untreated sucrose with 2% acetone solution (control/test item). The test item was intended to be applied once over 24 hours; the actual exposure time ranged between ~40 and 71 hours. **Mean colony size before exposure:** Control: 10 181 bees Treatments: 10 069 – 10 322 bees Reference toxicant: 9956 bees **Test duration:** 70 days (three brood cycles) Pre-application phase: 7 days Postapplication phase: 63 days **Number of replicates:** Four replicates/treatment group	colony development were assessed for up to 64 days after the application of the test item. Overall, no adverse effects on adult bee mortality and behaviour, colony strength or brood development were observed in bee colonies exposed orally to spiropidion up to a concentration of 32.0 ppm (37.66 mL test item in 1 L of sucrose solution with 2% acetone). An increase of pupal mortality was found in the highest test concentration group. This increase was only observed in one replicate and was therefore determined unlikely to be related to the test item. **Considerations:** The highest exposure concentration used in the study was higher than the maximum combined residue of spiropidion and SYN547305 (in parent equivalents) measured in nectar in the field residue studies (9.12 mg/kg measured in cucumber nectar in Italy following three applications of 160 g a.i./ha during bloom, with a 6 to 7 day interval. The maximum concentration was measured 1 DAA3 (PMRA No. 3436736). Exposure to spiropidion in nectar is most comparable to the mode of exposure for colonies used in the study (sucrose solution test media); however, the highest exposure concentration is lower than the maximum combined residue of spiropidion and SYN547305 (in parent equivalents) measured in pollen from the pollinator residue studies: • 90.3 mg/kg in cucumber pollen following three applications of 180 g a.i./ha, with a 7-day interval. The first application was applied pre-bloom while the remained two applications were applied during bloom (PMRA No. 3494921). • 512 mg/kg in apple pollen following two applications of 300 g a.i./ha via airblast with a 7-day retreatment interval. The first application was applied pre-bloom while the second was applied at early (10%) bloom (PMRA No. 3436737). • 32.7 mg/kg in tomato pollen following	

Study design	Summary and conclusions	PMRA No.
	two applications of 120 g a.i./ha with a 7-day retreatment interval (a total of four applications were used in the study). The applications were made during bloom (PMRA No. 3436739). Colony feeding studies allow bees to forage on alternate food sources which may dilute exposure. The exposure period was only up to 71 hours, which is shorter than the blooming period of many plants.	
Study type: Colony feeding study (Tier II) in North Carolina, USA; in-hive feeding method **Test species:** *Apis mellifera* L. **Crop:** N/A – test item was applied in-hive at a site with access to natural nectar and pollen sources. **Test item:** Spiropidion (98.3% purity) **Application rate and method:** 1 untreated control, 1 solvent control, and 3 dose rates of the test item (12.5, 25 and 50 ppm) The application was performed with an in-hive feeding method by providing 2 L treated/untreated sucrose with 2% acetone solution (control/test item) twice per week over a 6-week exposure period. **Mean colony size before exposure:** Control: 18 123 bees Treatments: 17 343 to 18 414 bees **Test duration:** 70 days (three brood cycles) Pre-application phase: 7 days Postapplication phase: 63 days **Number of replicates:** 13 replicates/treatment group (One hive/treatment was used for	A colony feeding study was conducted to evaluate chronic effects of an oral exposure of spiropidion (98.4% purity) on honeybee colonies. Free-foraging bee colonies were provided with two litres of treated/untreated sucrose with 2% acetone solution (control/test item) twice per week for six weeks. Test item application began 6 July 2021, and ended 13 August 2021. Assessments were made to evaluate the overall colony performance at several time points during and after the exposure period, as well as in the fall and following spring (in other words, after overwintering). Mortality, behaviour of bees, brood development and colony development were assessed for up to 64 days after the application of the test item. Bee bread (pollen) and nectar samples were collected throughout the study to monitor residues of spiropidion and its transformation product, SYN547305. The samples were stored frozen prior to analysis for up to 14.9 months, which exceeds the time that spiropidion is stable in frozen storage. Analysis of the stability samples in the study showed low levels of spiropidion while concentrations of SYN547305 were approaching the nominal test concentrations. As such, the combined residue of spiropidion and SYN547305 should be considered rather than spiropidion alone. Analysis of bee bread (pollen) and nectar samples showed that the control hives were exposed to low levels of spiropidion and/or	3465137

Study design	Summary and conclusions	PMRA No.
collection of pollen and nectar for residue monitoring purposes)	SYN547305 throughout the study (≤ 0.709 mg/kg). Residues of spiropidion and/or SYN547305 were measured in bee bread and nectar samples throughout the study (up to 37 weeks after exposure (WAE)). The concentrations of both analytes were higher in nectar/honey samples than in bee bread; concentrations of SYN547305 were generally higher than spiropidion in both matrices. Concentrations of spiropidion in bee bread samples reached maximum values of 0.0478, 0.0717 and 0.476 mg/kg in 12.5, 25 and 50 ppm treatments, respectively, while the maximum concentrations of SYN547305 were 1.40, 2.27 and 3.93 mg/kg (all measured at the end of feeding, 7 WAE). The concentrations of both analytes in bee bread decreased throughout the study. After over wintering (37 WAE), the maximum concentrations of spiropidion were <LOQ (0.010 mg/kg), 0.0265 mg/kg and <LOQ in the 12.5, 25 and 50 mg/kg treatments, respectively, while the maximum concentrations of SYN547305 were 0.0916, 0.512 and 0.562 mg/kg. In nectar/honey samples, the maximum concentrations of spiropidion were 0.113, 0.166 and 1.25 mg/kg in the 12.5, 25 and 50 ppm treatments, respectively, while the concentrations of SYN547305 were 2.80, 6.19 and 8.58 mg/kg. After over wintering (37 WAE), the maximum concentrations of spiropidion were 0.113, 0.0608 and 1.25 mg/kg in the 12.5, 25 and 50 ppm treatments, respectively, while the maximum concentrations of SYN547305 were 1.23, 3.97 and 5.52 mg/kg. The maximum concentrations of spiropidion in the nectar/honey from the end of exposure until after over wintering were variable: concentrations in the 12.5 ppm treatment were relatively stable from 7 WAE until 37 WAE, while they decreased in the 25 ppm treatment and increased in the 50 ppm treatment. The concentrations of SYN547305 slowly decreased during this period. Analyses of the colony condition assessment (CCA) data indicate apparent	

Study design	Summary and conclusions	PMRA No.
	effects on colony endpoints at the 50 ppm treatment. These effects were observed consistently at multiple time points at the highest dose tested. The effects observed in the 50 ppm treatment were evident for colony strength, pupae, total brood, nectar and pollen stores. These effects occurred at the middle of the dosing period (brood parameter), through the start of overwintering (nectar stores) or the following spring (pollen stores). At a single time point at CCA7 before overwintering, the number of total brood and egg cells were significantly lower in the 25 ppm treatment compared to the control; however, this is not considered to be due to the test item as a temporal or concentration-related response was not observed. During the test item feeding period, fall feeding and overwintering, the weight for all hives followed a similar pattern, increasing with fall feeding to a peak in November and decreasing over winter when food stores were consumed. After overwintering, the 50 ppm treatment hives exhibited a statistically significant weight difference compared to the pooled control hives in January and March 2022. The NOAEL and LOAEL for the study were determined to be 25 and 50 ppm, respectively. **Considerations**: A statistically significant effect on colony survival was not observed; however, all control colonies survived the winter while 75, 83 and 75% of the colonies in the 12.5, 25 and 50 ppm treatment groups, respectively, survived overwintering. It is unclear if exposure to spiropidion played a role in the colony deaths. The highest exposure concentration used in this study is higher than the maximum measured combined residue of spiropidion and SYN547305 in nectar from the field residue studies for pollinators, and lower than the measured pollen concentrations (see PMRA No. 3436784). The NOAEL and LOAEL are higher than the maximum	

Study design	Summary and conclusions	PMRA No.
	measured nectar concentration in the field residue studies. The control hives were exposed to low levels of spiropidion and/or SYN547305 in pollen and nectar throughout the study. Colony feeding studies allow bees to forage on alternate food sources which may dilute exposure.	

Table 26 Refined Tier II risk assessment for pollinators: Colony level risk

Crop	Use pattern	Sampling interval	Mean nectar (ppb)	Mean pollen (ppb)	RQs based on:			
					Mean nectar	Mean pollen	Mean nectar	Mean pollen
Effects metric					NOAEL = 25000 ppb[1]		LOAEL = 50000 ppb[1]	
Risk assessment based on the highest daily mean pollen and nectar values								
Cucumber	3 × 180 g a.i./ha, 7-d interval, applied 19, 12 and 5 days prior to bloom	7 ± 1 DAA3	62.1	1315	0.002	0.053	0.001	0.026
Cucumber	3 × 180 g a.i./ha, 7-d interval. 1st application was made prior to bloom, with the remaining two during bloom.	0 DAA3	591	42 862	0.024	**1.7**	0.012	0.86
Dry Bean	3 × 120 g a.i./ha, 7-d interval. 1st application was made at early bloom. Bloom was ending when last application was applied.	1 DAA2	959	87.4	0.038	0.003	0.019	0.002
	3 × 120 g a.i./ha, 7-d interval. 1st application 10 days after emergence, 2nd at early bloom and the 3rd at full bloom.	1 DAA3	1476	203	0.059	0.008	0.030	0.004
	3 × 75 g a.i./ha, 7-d interval. 1st application at early bloom. Bloom was ending when last application was applied.	1 DAA2	1317	122	0.053	0.005	0.026	0.002
Cucumber	2 × 160 g a.i./ha, 7-d interval. Final application just before bloom.	14 DAA2	594[2]	2484[2]	0.024	0.099	0.012	0.050
	3 × 160 g a.i./ha, 6 to 7-d interval. All three applications during bloom.	1 DAA3	7226[2]	18 460[2]	0.289	0.738	0.145	0.369
Apple	2 × 300 g a.i./ha, 7-day interval. 1st application before bloom, 2nd at early bloom (10% bloom)	1-2 DAA2	1114	375 530	0.045	**15**	0.022	**7.5**
Tomato	4 × 120 g a.i./ha, 7-day interval. All applications during bloom.	6 DAA2	N/A	27 579	N/A	**1.2**	N/A	0.55

Crop	Use pattern	Sampling interval	Mean nectar (ppb)	Mean pollen (ppb)	RQs based on:			
					Mean nectar	Mean pollen	Mean nectar	Mean pollen
Effects metric					NOAEL = 25000 ppb(1)		LOAEL = 50000 ppb(1)	
	3 × 60 g a.i./ha, 7-day interval. All applications during bloom. Test item was a co-formulation with acetamiprid.	1 DAA1	N/A	6663	N/A	0.27	N/A	0.13
Risk assessment based on the sampling events after the highest daily mean pollen and nectar values								
Cucumber	3 × 180 g a.i./ha, 7-d interval. 1st application was made prior to bloom, with the remaining two during bloom.	5 ± 2 DAA3	392	4059	0.012	0.16	0.006	0.081
Apple	2 × 300 g a.i./ha, 7-day interval. 1st application before bloom, 2nd at early bloom (10% bloom)	2 DAA2	1219	30144	0.049	**1.2**	0.024	0.60
		5 DAA2	487	25445	0.019	**1.0**	0.010	0.51
Tomato	3 × 60 g a.i./ha, 7-day interval. All applications during bloom. Test item was a co-formulation with acetamiprid.	1 DAA3	N/A	27579	N/A	**1.1**	N/A	0.55
		6 DAA3	N/A	21912	N/A	0.88	N/A	0.44

Bold: RQ exceeds the LOC of 1.
N/A – Not applicable because tomato plants do not produce nectar.
(1) The NOAEL and LOAEL are based on the spiropidion concentration in the sucrose feeding solutions used in the colony feeding study.
(2) Maximum residues were used since data were not available to calculate means. These RQs may overestimate risk to bee colonies.

Table 27 Uncertainties in the pollinator risk assessment

Area of the risk assessment	Uncertainties in the risk assessment
Field residue studies	• The application rates used in the field residue studies were variable. Only one study (cucumber; PMRA No. 3494921) used application rates that were the same as the maximum rate proposed for that crop in Canada (3 × 180 g a.i./ha, applied both before and during bloom). The cumulative application rate used in the apple residue study (PMRA No. 3436737) was consistent with the maximum yearly rate for pome fruit in Canada (600 g a.i./ha) with one application just before bloom and the second at 10% bloom; however, the single application rate was higher than what is proposed for Canada (300 g a.i./ha versus 200 g a.i./ha). The dry bean residue study (PMRA No. 3436734) and cucumber residue study (applied both before bloom and during bloom; PMRA No. 3436736) used rates that are lower than the maximum rates proposed in Canada. It is noted that dry bean is not a crop proposed for registration in Canada at this time, but residues were considered as weight of evidence/potential surrogate crop species. The tomato residue study (PMRA No. 3436739) used lower single application rates than those proposed in Canada; however, one of the treatments used an additional application (four applications versus the maximum of three in Canada). Considering the above, the residues from these studies may not be completely representative of the residues expected in Canadian crops when spiropidion is used at its maximum rate and may underestimate EECs in most cases. • One of the cucumber residue studies (PMRA No. 3436736) did not have data available to calculate mean residue concentrations for use in the chronic risk assessment. Given that the maximum and mean concentrations in the other residue studies were similar, the maximum concentrations were used to estimate the chronic RQs. This may overestimate the chronic risk; however, the effect is considered to be minimal. • There was significant variability in the measured concentrations of spiropidion and SYN547305 in nectar and pollen from the field residue studies. The maximum concentrations in a given crop were not always associated with highest application rate, nor were they measured directly following the application or after all applications of spiropidion (for example, in tomato crops, the highest concentrations in pollen were measured after the second of four spiropidion applications). • In the apple residue study, the first application was applied pre-bloom and the second application was applied at 10% bloom. A study where spiropidion was applied during full bloom, which may increase the risk, is not available.

Area of the risk assessment	Uncertainties in the risk assessment
Colony feeding study	• The colony feeding study used a constant exposure level to spiropidion/SYN547305 for 6 weeks. This may not be representative of field exposure where the actual level of exposure is expected to be a function of the foraging activity of bees, residue levels in crops and the bee-attractiveness of the crop. For example, pome fruit typically have a 2 to 3 week bloom period whereas cucurbit crops have an indeterminate bloom period and may bloom all season. • Following the end of 6-week exposure period, spiropidion and SYN547305 were measured in bee bread and nectar/honey samples from the spiropidion-treated bee colonies for at least 37 weeks. This indicates that exposure in the hive is not limited to the application period of spiropidion because residues may persist in the hive. • Feeding studies allow bees to forage on alternate food sources, which may dilute exposure to spiropidion and SYN547305. Pollen collected from the monitoring hives in the colony feeding study showed that the bees foraged on a number of species of plants; they are unlikely to be exposed exclusively to crops sprayed with spiropidion. Conversely, they could also be exposed to other pesticides on other crops which may also impact bee health. Pollen and nectar collected from monitoring hives in the 6-weekcolony feeding study show that the hives were exposed to several pesticides, including but not limited to, atrazine, carbendazim and diuron. The cumulative risk from exposure to multiple pesticides is not assessed here. • Analysis of bee bread and nectar samples from the control hives in the 6-week colony feeding study showed that they were exposed to low levels of spiropidion and SYN547305 throughout the study.
Colony level risk assessment	• RQs considering the results of the 6-week colony feeding study were calculated based on a single exposure route: pollen or nectar. In the field, bees forage on both pollen and nectar and can be simultaneously exposed to both. The exposure route (pollen or nectar) may affect how residues are distributed among hive food stores (bee bread, honey, royal jelly) thereby affecting at which stage bees may be exposed, and what effects may be observed in the colony. The NOAEL and LOAEL values from the colony feeding study were derived based on a single exposure route (sucrose solution), which would result in exposure through both honey and bee bread in the hive, introducing uncertainty into the risk assessment. It is unknown how the observed effects may be affected when bee colonies are exposed to spiropidion via a combination of both pollen and nectar. In this assessment, effects from nectar dosing were assumed to be equal to effects from pollen dosing/exposure. RQs for spiropidion only exceeded the LOC for exposure to pollen and not nectar. Exposure to nectar is more reflective of the sucrose route of exposure used in the study.

Table 28 Screening Level Risk Assessment for Birds and Mammals

Organism	Effects metric (mg a.i./kg bw/d)(1)	Feeding guild (food item)	EDE (mg a.i./kg bw)(2)	RQ(3)	LOC	LOC exceeded?
Small bird (0.02 kg)						
Acute	95.9	Insectivore	32.47	0.34	1	No
Reproduction	20.0	Insectivore	32.47	**1.6**	1	**Yes**
Medium-sized bird (0.1 kg)						
Acute	95.9	Insectivore	25.34	0.26		
Reproduction	20.0	Insectivore	25.34	**1.3**	1	**Yes**
Large-sized bird (1 kg)						
Acute	95.9	Herbivore (short grass)	16.37	0.17	1	No
Reproduction	20.0	Herbivore (short grass)	16.37	0.82	1	No
Small mammal (0.015 kg)						
Acute	> 200	Insectivore	18.68	< 0.09	1	No
Reproduction	24.0	Insectivore	18.68	0.78	1	No
Medium-sized mammal (0.035 kg)						
Acute	> 200	Herbivore (short grass)	36.22	< 0.18	1	No
Reproduction	24.0	Herbivore (short grass)	36.22	**1.5**	1	**Yes**
Large-sized mammal (1 kg)						
Acute	> 200	Insectivore	19.35	< 0.10	1	No
Reproduction	24.0	Insectivore	19.35	0.81	1	No

RQs that exceed the LOC are **bolded**

(1) To calculate the effects metric, uncertainty factors of 10 and 1 were applied to the acute oral (LD_{50}) and reproduction (NOED) endpoints, respectively.

(2) EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) × EEC, where:

FIR: Food Ingestion Rate (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:

Passerine Equation (body weight < or = 200 g): FIR (g dry weight/day) = 0.398 (bw in g) $^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648 (bw in g) $^{0.651}$

For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235 (bw in g) $^{0.822}$

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 3 × 200 g a.i./ha with a 7-day re-application interval and a default foliar half-life of 10 days.

(3) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 29 Refined risk assessment for birds and mammals exposed to spiropidion (6% Spray drift, field sprayer, medium droplet)

Exposure type	Effects metric (mg a.i./kg bw/d	Feeding guild	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ[(1)]	EDE (mg a.i./kg bw)	RQ[(1)]	EDE (mg a.i./kg bw)	RQ[(1)]	EDE (mg a.i./kg bw)	RQ[(1)]
Small bird (0.02 kg)										
Reproduction	20.0	Insectivore	32.5	**1.6**	1.95	0.10	22.4	**1.1**	1.35	0.07
	20.0	Granivore (grain and seeds)	5.03	0.25	0.30	0.02	2.40	0.12	0.14	0.01
	20.0	Frugivore (fruit)	10.1	0.50	0.60	0.03	4.79	0.24	0.29	0.01
Medium sized bird (0.1 kg)										
Reproduction	20.0	Insectivore	25.3	**1.3**	1.52	0.08	17.5	0.87	1.05	0.05
	20.0	Granivore (grain and seeds)	3.92	0.20	0.24	0.01	1.87	0.09	0.11	0.01
	20.0	Frugivore (fruit)	7.84	0.39	0.47	0.02	3.74	0.19	0.22	0.01
Large-sized bird (1 kg)										
Reproduction	20.0	Insectivore	7.40	0.37	0.44	0.02	5.11	0.26	0.31	0.02
	20.0	Granivore (grain and seeds)	1.14	0.06	0.07	0.003	0.55	0.03	0.03	0.002
	20.0	Frugivore (fruit)	2.29	0.11	0.14	0.007	1.09	0.05	0.07	0.003
	20.0	Herbivore (short grass)	16.4	0.82	0.98	0.05	5.81	0.29	0.35	0.02
	20.0	Herbivore (long grass)	9.99	0.50	0.60	0.03	3.26	0.16	0.20	0.01
	20.0	Herbivore (broadleaf plants)	15.1	0.76	0.91	0.05	5.01	0.25	0.30	0.02

Exposure type	Effects metric (mg a.i./kg bw/d	Feeding guild	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)
Small mammal (0.015 kg)										
Reproduction	24.0	Insectivore	18.7	0.78	1.12	0.05	12.90	0.54	0.77	0.03
	24.0	Granivore (grain and seeds)	2.89	0.12	0.17	0.007	1.38	0.06	0.08	0.003
	24.0	Frugivore (fruit)	5.78	0.24	0.35	0.01	2.76	0.11	0.17	0.007
Medium-sized mammal (0.035 kg)										
Reproduction	24.0	Insectivore	16.4	0.68	0.98	0.041	11.3	0.47	0.68	0.028
	24.0	Granivore (grain and seeds)	2.53	0.11	0.15	0.006	1.21	0.05	0.07	0.003
	24.0	Frugivore (fruit)	5.07	0.21	0.30	0.013	2.42	0.10	0.15	0.006
	24.0	Herbivore (short grass)	36.2	**1.5**	2.17	0.091	12.9	0.54	0.77	0.032
	24.0	Herbivore (long grass)	22.1	0.92	1.33	0.055	7.22	0.30	0.43	0.018
	24.0	Herbivore (Broadleaf plants)	33.5	**1.4**	2.01	0.084	11.1	0.46	0.66	0.028
Large-sized mammal (1 kg)										
Reproduction	24.0	Insectivore	8.75	0.36	0.52	0.02	6.04	0.25	0.36	0.015
	24.0	Granivore (grain and seeds)	1.35	0.06	0.08	0.003	0.65	0.027	0.04	0.002
	24.0	Frugivore (fruit)	2.71	0.11	0.16	0.007	1.29	0.054	0.08	0.003
	24.0	Herbivore (short grass)	19.4	0.81	1.16	0.048	6.87	0.29	0.41	0.017
	24.0	Herbivore (long grass)	11.8	0.49	0.71	0.030	3.86	0.16	0.23	0.01
	24.0	Herbivore (Broadleaf plants)	17.9	0.75	1.07	0.045	5.92	0.25	0.36	0.015

RQs that exceed the LOC are **bolded**

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 30 Refined Risk Assessment for Birds and Mammals Exposed to Spiropidion (74% Spray Drift, Early Season Airblast)

Exposure type	Effects metric (mg a.i./kg bw/d	Feeding guild	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]	EDE (mg a.i./kg bw)	RQ[1]
Small bird (0.02 kg)										
Reproduction	20.0	Insectivore	32.5	**1.6**	24.0	**1.2**	22.4	**1.1**	16.6	0.83
	20.0	Granivore (grain and seeds)	5.03	0.25	3.72	0.19	2.40	0.12	1.77	0.09
	20.0	Frugivore (fruit)	10.1	0.50	7.44	0.37	4.79	0.24	3.55	0.18
Medium-sized bird (0.1 kg)										
Reproduction	20.0	Insectivore	25.3	**1.3**	18.8	0.94	17.5	0.87	13.0	0.65
	20.0	Granivore (grain and seeds)	3.92	0.20	2.90	0.15	1.87	0.09	1.38	0.07
	20.0	Frugivore (fruit)	7.84	0.39	5.80	0.29	3.74	0.19	2.77	0.14
Large-sized bird (1 kg)										
Reproduction	20.0	Insectivore	7.40	0.37	5.47	0.27	5.11	0.26	3.78	0.19
	20.0	Granivore (grain and seeds)	1.14	0.06	0.85	0.04	0.55	0.03	0.40	0.02
	20.0	Frugivore (fruit)	2.29	0.11	1.69	0.08	1.09	0.05	0.81	0.04
	20.0	Herbivore (short grass)	16.4	0.82	12.1	0.61	5.81	0.29	4.30	0.22
	20.0	Herbivore (long grass)	9.99	0.50	7.40	0.37	3.26	0.16	2.41	0.12
	20.0	Herbivore (broadleaf plants)	15.1	0.76	11.2	0.56	5.01	0.25	3.70	0.19

Exposure type	Effects metric (mg a.i./kg bw/d	Feeding guild	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)
Small mammal (0.015 kg)										
Reproduction	24.0	Insectivore	18.7	0.78	13.8	0.58	12.9	0.54	9.54	0.40
	24.0	Granivore (grain and seeds)	2.89	0.12	2.14	0.09	1.38	0.057	1.02	0.04
	24.0	Frugivore (fruit)	5.78	0.24	4.28	0.18	2.76	0.11	2.04	0.09
Medium-sized mammal (0.035 kg)										
Reproduction	24.0	Insectivore	16.4	0.68	12.1	0.50	11.3	0.47	8.37	0.35
	24.0	Granivore (grain and seeds)	2.53	0.11	1.87	0.078	1.21	0.05	0.89	0.04
	24.0	Frugivore (fruit)	5.07	0.21	3.75	0.6	2.42	0.10	1.79	0.07
	24.0	Herbivore (short grass)	36.2	**1.5**	26.8	**1.1**	12.9	0.54	9.52	0.40
	24.0	Herbivore (long grass)	22.1	0.92	16.4	0.68	7.22	0.30	5.34	0.22
	24.0	Herbivore (Broadleaf plants)	33.5	**1.4**	24.8	**1.0**	11.1	0.46	8.20	0.34
Large-sized mammal (1 kg)										
Reproduction	24.0	Insectivore	8.75	0.36	6.47	0.29	6.04	0.25	4.47	0.19
	24.0	Granivore (grain and seeds)	1.35	0.056	1.00	0.04	0.65	0.03	0.48	0.02
	24.0	Frugivore (fruit)	2.71	0.11	2.00	0.08	1.29	0.05	0.96	0.04
	24.0	Herbivore (short grass)	19.4	0.81	14.3	0.60	6.87	0.29	5.09	0.21
	24.0	Herbivore (long grass)	11.8	0.49	8.75	0.36	3.86	0.16	2.86	0.12
	24.0	Herbivore (Broadleaf plants)	17.9	0.75	13.3	0.55	5.92	0.25	4.38	0.18

RQs that exceed the LOC are **bolded**

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 31 Refined risk assessment for birds exposed to spiropidion – Consideration of LOED value

Exposure type	Effects metric (mg a.i./kg bw/d	Feeding guild	Maximum nomogram residues				Mean nomogram residues			
			On-field		Off Field		On-field		Off Field	
			EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)	EDE (mg a.i./kg bw)	RQ(1)
6% Spray Drift (field sprayer, medium spray)										
Small bird (0.02 kg)										
Reproduction	60.0	Insectivore	32.5	0.54	1.95	0.03	22.4	0.37	1.35	0.02
	60.0	Granivore (grain and seeds)	5.03	0.08	0.30	0.01	2.40	0.04	0.14	0.002
	60.0	Frugivore (fruit)	10.1	0.17	0.60	0.01	4.79	0.08	0.29	0.005
Medium-sized bird (0.1 kg)										
Reproduction	60.0	Insectivore	25.3	0.42	1.52	0.03	17.5	0.29	1.05	0.02
	60.0	Granivore (grain and seeds)	3.92	0.07	0.24	0.00	1.87	0.03	0.11	0.002
	60.0	Frugivore (fruit)	7.84	0.13	0.47	0.01	3.74	0.06	0.22	0.004
74% Spray Drift (early air blast)										
Small bird (0.02 kg)										
Reproduction	60.0	Insectivore	32.5	0.54	24.0	0.40	22.4	0.37	16.6	0.28
	60.0	Granivore (grain and seeds)	5.03	0.08	3.72	0.06	2.40	0.04	1.77	0.03
	60.0	Frugivore (fruit)	10.1	0.17	7.44	0.12	4.79	0.08	3.55	0.06
Medium-sized bird (0.1 kg)										
Reproduction	60.0	Insectivore	25.3	0.42	18.8	0.31	17.50	0.29	13.0	0.22
	60.0	Granivore (grain and seeds)	3.92	0.07	2.90	0.05	1.87	0.03	1.38	0.02
	60.0	Frugivore (fruit)	7.84	0.13	5.80	0.10	3.74	0.06	2.77	0.05

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 32 Screening level risk assessment for aquatic organisms

Test organism	Exposure	Test substance	EEC (mg/L)	Endpoint (mg/L)	UF	Effects metric (mg/L)	RQ[(1)]	LOC of 1 exceeded?
Freshwater organisms								
Daphnia magna	48-h Acute	Spiropidion (SYN46330)	0.029	9.0	2	4.5	0.007	No
	48-h Acute	SYN547305	0.062	> 103	2	> 52	< 0.001	No
	21-d Chronic	Spiropidion (SYN46330)	0.029	0.32	1	0.32	0.092	No
Midge (*Chironomus riparius*)	48-h Acute (water exposure)	Spiropidion (SYN46330)	0.029	0.61	2	0.31	0.097	No
		SYN547305	0.062	> 7.1	2	> 3.6	< 0.018	No
		SYN548033	0.065	17	2	8.5	0.008	No
		SYN548274	0.059	> 101	2	> 51	< 0.001	No
		SYN548430	0.057	> 93	2	> 47	< 0.001	No
		SYN551480	0.046	> 94	2	> 47	< 0.001	No
		SYN552045	0.060	37	2	19	0.003	No
		SYN552257	0.055	> 89	2	> 45	< 0.001	No
Amphipod (*Hyalella azteca*)	10-d Sediment	Spiropidion (SYN46330)	0.029	> 0.93	2	> 0.47	< 0.063	No
Midge (*Chironomus dilutus*)	10-d Sediment	Spiropidion (SYN46330)	0.029	> 0.31	2	> 0.16	< 0.19	No
Rainbow trout (*Oncorhynchus mykiss*)	96-h Acute	Spiropidion (SYN46330)	0.029	0.56	10	0.056	0.53	No
		SYN547305	0.062	> 76	10	> 7.6	< 0.008	No
Common carp (*Cyprinus carpio*)	96h-Acute	Spiropidion (SYN46330)	0.029	1	10	0.10	0.30	No

Test organism	Exposure	Test substance	EEC (mg/L)	Endpoint (mg/L)	UF	Effects metric (mg/L)	RQ[(1)]	LOC of 1 exceeded?
Fathead minnow (*Pimephales promelas*)	96-h Acute	Spiropidion (SYN46330)	0.029	2.6	10	0.26	0.11	No
Fathead minnow (*Pimephales promelas*)	33-d Early life stage	Spiropidion (SYN46330)	0.029	0.11	1	0.11	0.27	No
Amphibians	96h-Acute (rainbow trout surrogate)	Spiropidion (SYN46330)	0.16	0.56	10	0.056	**2.8**	**Yes**
	96h-Acute (rainbow trout surrogate)	SYN547305	0.33	>76	10	7.6	<0.04	No
	Chronic (fathead minnow surrogate)	Spiropidion (SYN46330)	0.16	0.11	1	0.11	**1.4**	**Yes**
Freshwater algae (*Anabaena flos-aquae)*	96-h Acute	Spiropidion (SYN46330)	0.029	> 14	2	> 7.0	< 0.004	No
Freshwater diatom (Navicula pelliculosa*)*	96-h Acute	Spiropidion (SYN46330)	0.029	1.4	2	0.70	0.042	No
Freshwater algae (*Rhaphidocelis subcapitata*)	96-h Acute	Spiropidion (SYN46330)	0.029	4.1	2	2.1	0.014	No
	96-h Acute	SYN547305	0.029	27	2	14	0.002	No
Vascular plants (*Lemna gibba*)	7-d	Spiropidion (SYN46330)	0.029	1.4	2	0.70	0.042	No

Test organism	Exposure	Test substance	EEC (mg/L)	Endpoint (mg/L)	UF	Effects metric (mg/L)	RQ(1)	LOC of 1 exceeded?
Marine organisms								
Saltwater mysid (*Americamysis bahia*)	96-h Acute	Spiropidion (SYN46330)	0.029	2.9	2	1.5	0.020	No
	28-day Chronic	Spiropidion (SYN46330)	0.029	0.015	1	0.015	**2.0**	**Yes**
Eastern oyster (*Crassostrea virginica*)	96-h Acute	Spiropidion (SYN46330)	0.029	0.32	2	0.16	0.18	No
Amphipod (*Leptocheirus plumulosus*)	10-d Sediment	Spiropidion (SYN46330)	0.029	> 0.45	2	> 0.23	< 0.13	No
Sheepshead minnow (*Cyprinodon variegatus*)	96-h Acute	Spiropidion (SYN46330)	0.029	1.2	10	0.12	0.25	No
	34-d Early life stage	Spiropidion (SYN46330)	0.029	0.025	1	0.025	**1.2**	**Yes**
Marine diatom (*Skeletonema costatum*)	96-h Acute	Spiropidion (SYN46330)	0.029	0.39	2	0.20	0.15	No

Bold: RQ exceeds LOC

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 33 Refined spray drift risk assessment for aquatic organisms

Test organism	Exposure	Test substance	EEC (mg/L)	Endpoint (mg/L)	UF	Effects metric (mg/L)	RQ(1)	LOC of 1 exceeded?
6% Spray drift (field sprayer, medium spray)(2)								
Amphibians	96h-Acute (rainbow trout surrogate)	Spiropidion (SYN46330)	0.009	0.56	10	0.056	0.17	No

Test organism	Exposure	Test substance	EEC (mg/L)	Endpoint (mg/L)	UF	Effects metric (mg/L)	RQ(1)	LOC of 1 exceeded?
	Chronic (fathead minnow surrogate)	Spiropidion (SYN46330)	0.009	0.11	1	0.11	0.09	No
74% Spray drift (early season airblast) (2)								
Amphibians	96h-Acute (rainbow trout surrogate)	Spiropidion (SYN46330)	0.12	0.56	10	0.056	**2.1**	**Yes**
	Chronic (fathead minnow surrogate)	Spiropidion (SYN46330)	0.12	0.11	1	0.11	**1.1**	**Yes**

Bold: RQ exceeds LOC

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

(2) Chronic exposure is not expected to occur as a result of spray drift to the estuarine/marine environment. See Section 4.2.2 for further details.

Table 34 Runoff EECs in Surface Water

Crop	Use pattern (g a.i./ha)	Region	Water column EEC – 15 cm (µg a.i./L)			Water column – 80 cm (µg a.i./L)		
			24-h	96-h	21-d	24-h	96-h	21-d
Apples	Airblast: 3 × 200 (7-day interval)	British Columbia	4.5	3.7	1.5	0.9	0.7	0.3
		Ontario	27	22	9.3	5.2	4.3	1.9
		Quebec	23	19	8.8	4.4	3.7	1.8
		Nova Scotia	24	19	8.2	4.5	3.8	1.7
Broccoli	Ground application: 3 × 180 (7-day interval)	British Columbia	4.5	3.6	1.5	0.9	0.7	0.3
		Alberta	26	21	8.9	5.0	4.2	1.9
		Manitoba	32	26	11	6.3	5.2	2.4
		Ontario	38	31	14	7.2	6.1	2.8
		Quebec	31	25	13	6.0	5.0	2.8
		Prince Edward Island	70	62	29	14	13	6.4
Tomatoes		British Columbia	2.2	1.8	0.8	0.4	0.4	0.2
		Ontario	36	31	14	7.0	6.2	3.0
		Quebec	27	22	11	5.4	4.5	2.2
Pumpkin		Alberta	20	18	7.4	3.9	3.5	1.6
		Manitoba	32	26	11	6.3	5.2	2.4
		Prince Edward Island	**101**	**82**	**34**	**21**	**17**	**7.8**

Maximum EECs are shown in **bold.**

The fate parameters used in the runoff modelling are as follows: K_d value of 1.40 L/kg; K_{OC} value of 76.8 L/kg (20th percentile of seven values available for spiropidion); hydrolysis half-life of 5.5 days at 25°C (pH 7); soil half-life of 1.5 days at 25°C (90% upper confidence bound on the mean of five soils). Spiropidion was considered to be stable for the water column metabolism, benthic metabolism and aqueous photolysis half-lives because it undergoes rapid hydrolysis.

Table 35 Runoff Risk Assessment for Aquatic Organisms

Test organism	Exposure	Test substance	EEC (mg a.i./L)	Endpoint (mg a.i./L)	UF	Effects metric (mg a.i./L)	RQ[(1)]	LOC of 1 exceeded?
Runoff								
Amphibians	96h-Acute (rainbow trout surrogate)	Spiropidion (SYN46330)	0.10	0.56	10	0.056	**1.8**	**Yes**
	Chronic (fathead	Spiropidion (SYN46330)	0.034	0.11	1	0.11	0.31	No

Test organism	Exposure	Test substance	EEC (mg a.i./L)	Endpoint (mg a.i./L)	UF	Effects metric (mg a.i./L)	RQ(1)	LOC of 1 exceeded?
	minnow surrogate)							
Saltwater mysid (*Americamysis bahia*)	28-day Chronic	Spiropidion (SYN46330)	0.0078	0.015	1	0.015	0.52	No
Sheepshead minnow (*Cyprinodon variegatus*)	34-d Early life stage	Spiropidion (SYN46330)	0.0078	0.025	1	0.025	0.31	No

Bold: RQ exceeds LOC

(1) RQs were calculated using Microsoft Excel. Values in this table have been rounded for presentation which may result in minor discrepancies in RQs calculated based on the values presented in this table.

Table 36 Use (label) claims proposed by applicant and whether acceptable or unsupported

Supported claim
Leafy Vegetables (excluding watercress): Control of aphids and whiteflies: • Foliar application at a rate of 0.3 to 0.6 L product per ha (90 to 180 g a.i. per ha) in a minimum water volume of 200 L per ha. Apply with a methylated seed oil adjuvant at 0.1 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 3 applications with a minimum reapplication interval of 7 days may be made per year, however the number of consecutive sprays is limited to 2.
Crop Group 5-13 Brassica Head and Stem Vegetables: Control of aphids and whiteflies: • Foliar applications at a rate of 0.3 to 0.6 L product per ha (90 to 180 g a.i. per ha) in a minimum water volume of 200 L per ha. Apply with a methylated seed oil adjuvant at 0.1 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 3 applications with a minimum reapplication interval of 7 days may be made per year, however the number of consecutive sprays is limited to 2.
Crop Group 8-09 Fruiting Vegetables: Control of aphids and whiteflies: • Foliar applications at a rate of 0.3 to 0.6 L product per ha (90 to 180 g a.i. per ha) in a minimum water volume of 200 L per ha. Apply with a methylated seed oil adjuvant at 0.1 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 3 applications with a minimum reapplication interval of 7 days may be made per year, however the number of consecutive sprays is limited to 2.

Supported claim
Crop Group 9 Cucurbit Vegetables: Control of aphids and whiteflies: • Foliar applications at a rate of 0.3 to 0.6 L product per ha (90 to 180 g a.i. per ha) in a minimum water volume of 200 L per ha. Apply with a methylated seed oil adjuvant at 0.1 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 3 applications with a minimum reapplication interval of 7 days may be made per year, however the number of consecutive sprays is limited to 2.
Crop Group 11-09 Pome Fruits: Suppression of aphids: • Foliar airblast applications at a rate of 0.33 to 0.67 L product per ha (100 to 200 g a.i. per ha) in a water volume of 400 to 4000 L per ha. Apply with a methylated seed oil adjuvant at 0.05 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 3 applications with a minimum reapplication interval of 7 days may be made per year, however, the number of consecutive sprays is limited to 2.
Grapes: Control of mealybugs: • Foliar airblast applications at a rate of 0.5 to 0.67 L product per ha (150 to 200 g a.i. per ha) in a water volume of 500 to 1000 L per ha. Apply with a methylated seed oil adjuvant at 0.05 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 3 applications with a minimum reapplication interval of 7 days may be made per year, however the number of consecutive sprays is limited to 2.
Greenhouse tomatoes, peppers, eggplant, and cucumbers: Control of aphids, whiteflies and two-spotted spider mites: • Foliar applications at a rate of 0.3 to 0.48 L product per ha (90 to 144 g a.i. per ha) in a water volume of 300 to 2000 L per ha. Apply with a methylated seed oil adjuvant at 0.05 to 0.25% v/v. Apply the higher rate under high pest populations. • A maximum of 2 applications with a minimum reapplication interval of 7 days may be made per year.

Table 37 Toxic substances management policy considerations - Comparison to TSMP track 1 criteria

TSMP track 1 criteria	TSMP track 1 criterion value		Spiropidion endpoints	Transformation Products (TP) endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes	Yes
Predominantly anthropogenic[2]	Yes		Yes	Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	No Total system (water + sediment):	*All DT_{50} values are for total system (water + sediment)

TSMP track 1 criteria	TSMP track 1 criterion value		Spiropidion endpoints	Transformation Products (TP) endpoints
			Aerobic DT_{50} values: 0.26 to 1.11 days Anaerobic DT_{50} values: 0.29 to 0.71 days	**SYN547305**: Yes, in anaerobic systems Aerobic DT_{50} values: 0.13 to 17.1 days Anaerobic DT_{50} values: 165 to 839 days **SYN548430:** Biotransformation in soil half-lives are not available for this TP. **SYN548274:** Biotransformation in soil half-lives are not available for this TP. **SYN552045:** No Aerobic DT_{50} values: 22.17 to 38.91 days Anaerobic DT_{50} values: Not available. **SYN548037:** No Aerobic DT_{50} values: 2.94 to 5.20 days Anaerobic DT_{50} values: Not available. **SYN551480:** Biotransformation in soil half-lives are not available for this TP. **SYN552257:** No Aerobic DT_{50} values: 1.57 to 7.80 days Anaerobic DT_{50} values: Not available. **SYN548033:** No Aerobic DT_{50} values: 5.85 to 19.4 days Anaerobic DT_{50} values: Not available.
	Water	Half-life ≥ 182 days	No Total system aerobic DT_{50} values: <3 days Total system anaerobic DT_{50} values: <0.1 days	**SYN547305**: Yes Aerobic DT_{50} values: 485 and 495 days Anaerobic DT_{50} values: 305 and 498 days
	Sediment	Half-life ≥ 365 days		

TSMP track 1 criteria	TSMP track 1 criterion value		Spiropidion endpoints	Transformation Products (TP) endpoints
				SYN548430, SYN548274, SYN552045, SYN548037, SYN551480, SYN552257, SYN548033: Aquatic biotransformation half-lives for aquatic biotransformation are not available for these TPs.
	Air	Half-life ≥ 2 days, or evidence of atmospheric transport to remote regions such as the Arctic	Not determined. The AOPWIN model (v1.92) is not suited for predicting the atmospheric half-life of spiropidion given the large fraction expected to be sorbed to airborne particles.	**SYN548037:** Yes, the AOPWIN (v1.92) predicted half-life in the gas phase in the atmosphere is 2.52 days based on the hydroxyl (OH) radical reaction (1.5×10^6 molecules OH/cm^3) during t12 hours of daylight. **SYN547305, SYN548430, SYN548274, SYN551480, SYN552045, SYN552257, SYN548033:** Not determined. The AOPWIN model (v1.92) is not suited for predicting the atmospheric half-life of these transformation products given the large fraction expected to be sorbed to airborne particles.
Bioaccumulation[4]	Log K_{OW} ≥ 5		No, Log K_{OW} = 3.3	No, Log K_{OW}: **SYN547305**: ≤ 2.54 **SYN548430:** ≤ -0.082 **SYN548274:** 0.829 **SYN552045:** ≤ 2.64 **SYN548037:** ≤ 0.925 **SYN551480: < -**4.40 **SYN552257: ≤** -0.445 **SYN548033:** 3.06
	BCF ≥ 5000		No, lipid normalized, growth corrected kinetic bioconcentration factor, BCF_{KgL}, = 53.4 *BCF applies to the combined residue of spiropidion and SYN547305	Not Required based on log K_{OW} values
	BAF ≥ 5000		Not required	Not required
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet all of the TSMP Track 1 criteria.	No, does not meet all of the TSMP Track 1 criteria for the major TPs.

TSMP track 1 criteria	TSMP track 1 criterion value	Spiropidion endpoints	Transformation Products (TP) endpoints

[1] All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).
[2] The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] The pesticide and/or the transformation product(s) is considered persistent when the criterion is met in any one medium.
[4] Bioaccumulation describes the process by which a substance accumulates in a living organism - either from the surrounding medium or through food containing the substance. A substance's potential to bioaccumulate can be expressed by the bioaccumulation factor (BAF), the bioconcentration factor (BCF), or the octanol-water partition coefficient (Log K_{OW}). The BAF and the BCF measure the concentration of a substance in a living organism relative to its concentration in the surrounding medium. The BAF accounts for substance intake from both food and the surrounding medium, while the BCF accounts for intake from the surrounding medium only. The Log K_{OW} estimates a substance's tendency to partition from water to organic media, such as lipids present in living organisms. In the absence of BAF or BCF data, the log K_{OW} may be used.

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

Spiropidion is an active ingredient that is concurrently being registered in Canada and the United States for use on tuberous and corm vegetables (CSG 1C), leafy vegetables (CG 4-13, excluding watercress), Brassica head and stem vegetables (CG 5-13), fruiting vegetables (CG 8-09), cucurbit vegetables (CG 9), citrus fruits (CSG 10A/B/C), pome fruit (CG 11-09), small fruits vine climbing except fuzzy kiwifruit (CSG 13-07F), cottonseeds (CSG 20C), and soybean. The MRLs proposed for spiropidion in Canada are the same as corresponding tolerances to be promulgated in the United States.

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

Currently, there are Codex MRLs[11] listed for spiropidion in or on various individual crop commodities on the Codex Alimentarius Pesticide Index website.

Table 1 compares the MRLs proposed for spiropidion in Canada with corresponding American tolerances (where different).

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

Food commodity	Canadian MRL (ppm)	American tolerance (ppm)
Wine	5	Not proposed
Meat byproducts of cattle, goat, horse, sheep	Not proposed	0.2
Fat of cattle, goat, horse, sheep	Not proposed	0.02

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

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

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
3161276	2020, Spiropidion Technical (SYN546330) - Document MII, Section 1, DACO: 0.9.1,10.2.1,10.2.2, 10.2.3,10.5.3,10.6,12.7,2.1,2.10,2.11.1,2.11.2,2.11.3, 2.11.4, 2.12.1, 2.12.2,2.13.2,2.13.3,2.13.4, 2.14.1,2.14.10, 2.14.12,2.14.13, 2.14.14, 2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7,2.14.8,2.14.9,2.16,2.2,2.3,2.3.1,2.4,2.5, 2.6,2.7,2.8,2.9,8.2.3.2,8.4.1,8.6,Document M,IIA 1.1,IIA 1.10.1,IIA 1.10.2,IIA 1.11.1,IIA 1.11.2,IIA 1.2,IIA 1.3,IIA 1.4,IIA 1.5.1,IIA 1.5.2,IIA 1.5.3,IIA 1.6,IIA 1.7,IIA 1.8.1,IIA 1.9.1.1,IIA 1.9.1.2,IIA 2.1.1,IIA 2.1.2,IIA 2.11.1,IIA 2.12,IIA 2.13,IIA 2.14,IIA 2.15,IIA 2. CBI
3161282	2020, Spiropidion Technical (SYN546330) - Physico-Chemical Studies of the Pure and Technical Substance, DACO: 2.13.2,2.14.1,2.14.10, 2.14.11, 2.14.12, 2.14.13,2.14.14, 2.14.2,2.14.3,2.14.4,2.14.5, 2.14.6,2.14.7,2.14.8, 2.14.9, 2.16, 8.2.3.2,IIA 2.1.1,IIA 2.1.2,IIA 2.1.3,IIA.CBI
3161273	2020, Spiropidion Technical (SYN546330) - Document J - Confidential Information, DACO: 0.8.11,0.8.12,2.11.1,2.11.2, 2.11.3,2.11.4,2.12.1,2.12.2 ,2.13.3,2.13.4,2.2, 4.2.9,4.3.8,4.4.5,4.5.8,4.8,Document J,IIA 1.10.1,IIA 1.10.2,IIA 1.11.1,IIA 1.11.2,IIA 1.2,IIA 1.8.1,IIA 1.8.2,IIA. CBI
3436586	2022, Spiropidion Technical (SYN546330) - Document J - Confidential Information, DACO: 2.11.1,2.11.2,2.11.3, 2.11.4,2.12.1,2.12.2,2.13.2, 2.13.3,2.13.4,2.14.12,Document J,IIA 1.10.1,IIA 1.10.2,IIA 1.11.1,IIA 1.11.2,IIA 1.2,IIA 1.8.1,IIA 1.8.2,IIA 1.9.1,IIA 1.9.2,IIA 1.9.3,IIA. CBI
3711746	2025, Confidential Business Information Spiropidion Technical Insecticide Reg. No. Pending, DACO: 2.11.3,2.12 CBI
3492183	2023, Spiropidion Technical (SYN546330) - Manufacturing Process Description and Supporting Data, DACO: 2.1,2.11,2.11.1,2.11.2,2.11.3,2.11.4, 2.12,2.12.1,2.13,2.13.1,2.13.2,2.13.3, 2.13.4,2.2,2.3,2.4,2.5,2.6,2.7,2.8,2.9 CBI
3365284	2022, Spiropidion Technical (SYN546330) - Document J - Confidential Information - Addendum to 2020-4760, DACO: 0.8.11,0.8.12,2.13.3,Document J,IIA 1.11.1 CBI
3161283	2020, Analytical Method SA-134/1-Determination of Spiropidion in Spiropidion by HPLC., DACO: 2.13.1,IIA 4.2.1 CBI
3161284	2017, Spiropidion - Validation of Analytical Method SA-134/1, DACO: 2.13.1,IIA 4.2.1 CBI
3492182	2023, Confirmation of Identity Spiropidion Technical, DACO: 2.13.2. CBI

3775075	2025, Quality Control Data for Spiropidion, DACO: 2.16 CBI
3775076	2025, Quality Control Data for Spiropidion, DACO: 2.16 CBI
3436598	2017, SYN546330 - Analytical Method GRM069.03A for the Determination of SYN546330 and its Metabolite SYN547305 in Pollen and Nectar by LC-MS/MS, DACO: 8.2.2.4,IIA 4.3
3436601	2022, SYN546330 Independent Laboratory Validation of Analytical Method GRM069.03A for the Determination of SYN546330 and its Metabolite SYN547305 in Pollen and Nectar by LC-MS/MS, DACO: 8.2.2.4,IIA 4.3
3436602	2017, SYN546330 Validation of the Analytical Method GRM069.03A for the Determination of Residues of SYN546330 and its Metabolite SYN547305 in Pollen and Nectar by LC-MS/MS, DACO: 8.2.2.4,IIA 4.3
3436607	2018, SYN546330 - Analytical Method GRM069.05A for the Determination of SYN546330 and its Metabolites SYN547305, SYN548033, SYN549098 & SYN549979 in Soil, DACO: 8.2.2.1,IIA 4.4
3436608	2022, Independent Laboratory Validation: SYN546330 - Analytical Method GRM069.05A for the Determination of SYN546330 and its Metabolites SYN547305, SYN548033, SYN549098 & SYN549979 in Soil, DACO: 8.2.2.1,IIA 4.4
3436609	2022, Independent Laboratory Validation: SYN546330 - Analytical Method GRM069.13A for the Determination of SYN548037, SYN548430 and SYN550839 in Soil, DACO: 8.2.2.1,IIA 4.4
3436610	2022, Independent Laboratory Validation: SYN546330 Analytical Method GRM069.19A for the Determination of SYN546330 Metabolites SYN552045 and SYN552257 in Soil, DACO: 8.2.2.1,IIA 4.4
3436611	2020, SYN546330 - Analytical Method GRM069.13A for the Determination of SYN548037, SYN548430 and SYN550839 in Soil, DACO: 8.2.2.1,IIA 4.4
3436612	2021, SYN546330 - Analytical Method GRM069.19A for the Determination of SYN546330 Metabolites SYN552045 and SYN552257 in Soil, DACO: 8.2.2.1,IIA 4.4
3436613	2018, Method Validation for - "SYN546330 - Analytical Method GRM069.05A for the Determination of SYN546330 and its Metabolites SYN547305, SYN548033, SYN549098 & SYN549979 in Soil", DACO: 8.2.2.1,IIA 4.4
3436614	2020, SYN546330 - Validation of Analytical Method GRM069.13A for the Determination of SYN548037, SYN548430 and SYN550839 in Soil, DACO: 8.2.2.1,IIA 4.4
3436615	2021, SYN546330 - Validation of Analytical Method GRM069.19A for the Determination of SYN552045 and SYN552257 in Soil, DACO: 8.2.2.1,IIA 4.4
3436616	2018, SYN546330 - Analytical Method (GRM069.06A) for the Determination of SYN546330 and its Metabolite SYN547305 in Water, DACO: 8.2.2.3,IIA 4.5

3436617	2018, SYN546330 - Validation of Analytical Method (GRM069.06A) for the Determination of SYN546330 and its Metabolite SYN547305 in Water, DACO: 8.2.2.3,IIA 4.5
3436618	2021, SYN546330 - Independent Laboratory Validation of Analytical Method (GRM069.06A) for the Determination of SYN546330 and its Metabolite SYN547305 in Water, DACO: 8.2.2.3,IIA 4.5
3436619	2022, Analytical Method Validation ECO_071_02A for the Determination of SYN546330 and Its Metabolite SYN547305 in Formulated and Natural Marine Sediments, DACO: 8.2.2.2,IIA 4.6
3436622	2018, SYN547305 - Analytical Method ECO_071_01E and Validation for the Determination of SYN547305 in Freshwater, DACO: 8.2.2.3,IIA 4.9
3436623	2021, Validation of the Analytical Method ECO_071_01N for the Determination of SYN548033 in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436624	2021, Validation of the Analytical Method ECO_071_01P for the Determination of SYN548274 in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436625	2021, Validation of the Analytical Method ECO_071_01O for the Determination of SYN548430 in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436626	2021, Validation of the Analytical Method ECO_071_01M for the Determination of SYN549098 in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436627	2021, Validation of the Analytical Method ECO_071_01L for the Determination of SYN550839 in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436628	2021, SYN551480 - Validation of the Analytical Method ECO_071_01S for Determination in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436629	2021, SYN552045 - Validation of the Analytical Method ECO_071_01R for Determination in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3436630	2021, SYN552257 - Validation of the Analytical Method ECO_071_01Q for Determination in Aquatic Ecotoxicology Test Medium, DACO: 8.2.2.3,IIA 4.9
3161386	2020, A20262B - Physico-Chemical Studies of the Formulation, DACO: 3.5.1,3.5.10,3.5.11,3.5.12,3.5.14,3.5.2,3.5.3,3.5.6,3.5.7,3.5.8,3.5.9,3.7,IIIA 2.1,IIIA 2.15,IIIA 2.2.1,IIIA 2.2.2,IIIA 2.3.1,IIIA 2.3.2,IIIA 2.4.2,IIIA 2.5.2,IIIA 2.6.1,IIIA 2.7.1,IIIA 4.1.3 CBI
3161274	2020, A20262B - Document J - Confidential Information, DACO: 3.1.2,3.2.1,3.2.2,3.2.3,Document J,IIIA 1.2.1,IIIA 1.2.2,IIIA 1.4.1,IIIA 1.4.2,IIIA 1.4.4,IIIA 1.4.5.1,IIIA 1.4.5.2,IIIA 5.2.4,IIIA 5.2.5,IIIA 7.9.1,IIIA 7.9.2 CBI
3161387	2016, A20262B - Validation of Analytical Method SF-877/1, DACO: 3.4.1,IIIA 5.2.1 CBI

3161388	2020, Analytical Method SF-877/1 - Determination of SYN546330 in Formulation SC (300) by HPLC, DACO: 3.4.1,IIIA 5.2.1 CBI

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PMRA Document Number	Reference
3161389	2017, SYN546330 SC (A20262B) - Acute Oral Toxicity Study in Rats (Up and Down Procedure), DACO: 4.6.1,IIIA 7.1.1
3436476	2017, SYN546330 SC (A20262B) - Acute Dermal Toxicity Study in Rats, DACO: 4.6.2,IIIA 7.1.2
3436477	2021, SYN546330 SC (A20262B) - Acute Inhalation Toxicity Study (Nose-Only) in Rats, DACO: 4.6.3,IIIA 7.1.3
3436480	2017, SYN546330 SC (A20262B) - Acute Eye Irritation Study in Rabbits, DACO: 4.6.4,IIIA 7.1.5
3436481	2017, SYN546330 SC (A20262B) - In Vitro Eye Irritation Test in Isolated Chicken Eyes, DACO: 4.6.4,IIIA 7.1.5
3436478	2017, SYN546330 SC (A20262B) - In Vitro Skin Irritation Test in the EPISKIN Model, DACO: 4.6.5,IIIA 7.1.4
3436479	2017, SYN546330 SC (A20262B) - Primary Skin Irritation Study in Rabbits, DACO: 4.6.5,IIIA 7.1.4
3436482	2018, SYN546330 SC (A20262B) - Local Lymph Node Assay (LLNA) in Mice, DACO: 4.6.6,IIIA 7.1.6
3161295	2016, SYN546330 - The Absorption and Excretion of [14C]-SYN546330 Following Single Oral and Intravenous Administration in the Rat, DACO: 4.5.9,IIA 5.1.1
3161296	2018, SYN546330 - In Vitro Rat and Human Liver Microsomal Metabolism, DACO: 4.5.9,IIA 5.1.1
3161297	2016, SYN546330 - Pharmacokinetics of [14C]-SYN546330 Following Single Oral and Intravenous Administration in the Rat, DACO: 4.5.9,IIA 5.1.1
3161298	2019, Pharmacokinetics of SYN546330 and CSCD710959 in the Rat Following Single Oral and Intravenous Administration and Multiple Oral Administration, DACO: 4.5.9,IIA 5.1.1
3161299	2016, SYN546330 - Tissue Depletion of [14C]-SYN546330 Following Single Oral Administration in the Rat, DACO: 4.5.9,IIA 5.1.1
3161300	2017, SYN546330 - Biotransformation of [14C]- SYN546330 in Rat, DACO: 4.5.9,IIA 5.1.1

3161301	2016, SYN546330 - A Preliminary Study of Pharmacokinetics, Absorption, Metabolism and Excretion in the Rat Following Single Oral and Intravenous Administration of [Phenyl-U-14C] and [Spirodecanone-5-14C]-SYN546330, DACO: 4.5.9,IIA 5.1.1
3161302	2020, Spiropidion - Waiver Request for a 28-Day Immunotoxicity Study in Rodents, DACO: 4.2.9,4.3.8,4.4.5,4.5.8,4.8,IIA 5.10
3161303	2019, Spiropidion - In Vitro 3T3 NRU Phototoxicity Test, DACO: 4.2.9,4.3.8,4.4.5,4.5.8,4.8,IIA 5.10
3161304	2017, SYN546330 - Acute Oral Toxicity Study in Rat (Up and Down Procedure), DACO: 4.2.1,IIA 5.2.1
3161305	2020, SYN547435 - Acute Oral Toxicity Study in Rats (Up and Down Procedure), DACO: 4.2.1,IIA 5.2.1
3161306	2016, SYN546330 - Acute Dermal Toxicity Study in Rat, DACO: 4.2.2,IIA 5.2.2
3161307	2017, SYN546330 - Acute Inhalation Toxicity Study (Nose-Only) in the Rat, DACO: 4.2.3,IIA 5.2.3
3161308	2015, SYN546330 - Primary Skin Irritation Study in Rabbits, DACO: 4.2.5,IIA 5.2.4
3161309	2016, SYN546330 - Acute Eye Irritation Study in Rabbits, DACO: 4.2.4,IIA 5.2.5
3161310	2015, SYN546330 - In Vitro Eye Irritation Test in Isolated Chicken Eyes, DACO: 4.2.4,IIA 5.2.5
3161311	2015, SYN546330 - Local Lymph Node Assay in the Mouse, DACO: 4.2.6,IIA 5.2.6
3161312	2018, SYN546330 - A 28 Day Oral (Dietary) Toxicity Study in Mice, DACO: 4.3.3,IIA 5.3.1
3161313	2018, SYN546330 - A 28 Day Toxicity Study by Oral (Capsule) in Dogs, DACO: 4.3.3,IIA 5.3.1
3161314	2014, SYN546330 - 28 Day Toxicity Study in the Rat, DACO: 4.3.3,IIA 5.3.1
3161315	2018, SYN546330 - 13 Week Dietary Toxicity Study in Rats, DACO: 4.3.1,IIA 5.3.2
3161316	2018, SYN546330 - 13 Week Oral (Dietary) Toxicity Study in Mice, DACO: 4.3.1,IIA 5.3.2
3161317	2020, Supplemental Data to Support SYN546330 - 13 Week Dietary Toxicity Study in Rats, DACO: 4.3.1,IIA 5.3.2
3161318	2020, Supplemental Data to Support SYN546330 - 13 Week Oral (Dietary) Toxicity Study in Mice, DACO: 4.3.1,IIA 5.3.2

3161319	2018, SYN546330 - 13 Week Oral (Capsule) Toxicity Study in the Dog, DACO: 4.3.2,IIA 5.3.3
3161321	2018, SYN546330 - 52 Week Oral (Capsule) Toxicity Study in Dogs, DACO: 4.3.2,IIA 5.3.4
3161322	2018, SYN546330 - Toxicity Study by Dermal Administration to Han Wistar Rats for 4 Weeks, DACO: 4.3.5,IIA 5.3.7
3161323	2018, SYN546330 - Bacterial Reverse Mutation Assay - Ames Test using Salmonella typhimurium and Escherichia coli, DACO: 4.5.4,IIA 5.4.1
3161324	2014, SYN546330 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay, DACO: 4.5.4,IIA 5.4.1
3161325	2015, SYN546330 - Chromosome Aberration Test in Human Lymphocytes In Vitro, DACO: 4.5.5,IIA 5.4.3
3161326	2018, SYN546330 - Micronucleus Test in Human Lymphocytes In Vitro, DACO: 4.5.6,IIA 5.4.2
3161327	2015, SYN546330 - Cell Mutation Assay at the Thymidine Kinase Locus (TK+/-) in Mouse Lymphoma L5178Y Cells, DACO: 4.5.6,IIA 5.4.2
3161328	2018, SYN546330 - Rat Bone Marrow Chromosome Aberration Assay, DACO: 4.5.7,IIA 5.4.4
3161329	2018, SYN546330 - Oral (Gavage) Rat Micronucleus Test, DACO: 4.5.7,IIA 5.4.4
3161330	2015, SYN546330 - Oral (Gavage) Rat Micronucleus Test, DACO: 4.5.7,IIA 5.4.4
3161331	2018, SYN546330 - 104 Week Rat Oral (Dietary) Carcinogenicity Study with a Combined 52 Week Toxicity Study, DACO: 4.4.1,4.4.4,IIA 5.5.1
3161332	2020, Supplemental Data to Support SYN546330 - 104 Week Rat Oral (Dietary) Carcinogenicity Study with a Combined 52 Week Toxicity Study, DACO: 4.4.1,4.4.4,IIA 5.5.1
3161333	2020, Supplemental Data to Support SYN546330 - 80 Week Mouse Oral (Dietary) Carcinogenicity Study, DACO: 4.4.3,IIA 5.5.3
3161334	2018, SYN546330 - 80 Week Mouse Oral (Dietary) Carcinogenicity Study, DACO: 4.4.3,IIA 5.5.3
3161335	2014, SYN546330 - Assessment of UDP-Glucuronosyltransferase Induction Following a 13-Week Dietary Toxicity Study in Han Wistar Rats, DACO: 4.8,IIA 5.5.4
3161338	2014, SYN546330 and SYN547305 - Effect on Rat Thyroid Peroxidase Activity In Vitro, DACO: 4.8,IIA 5.5.4
3161339	2019, SYN546330 - Oral (Dietary) Two-Generation Reproduction Toxicity Study in the Rat, DACO: 4.5.1,IIA 5.6.1

3161340	2020, Supplemental Data to Support SYN546330 - Oral (Dietary) Two-Generation Reproduction Toxicity Study in the Rat, DACO: 4.5.1,IIA 5.6.1
3161341	2016, SYN546330 - Oral (Gavage) Preliminary Prenatal Developmental Toxicity Study in the Rat, DACO: 4.5.2,IIA 5.6.10
3161342	2017, SYN546330 - Oral (Gavage) Prenatal Developmental Toxicity Study in the Rat, DACO: 4.5.2,IIA 5.6.10
3161343	2016, SYN546330 - Oral (Gavage) Tolerability Study in the Non-Pregnant Rat, DACO: 4.5.2,IIA 5.6.10
3161344	2020, Supplemental Data to Support SYN546330 - Oral (Gavage) Prenatal Developmental Toxicity Study in the Rat, DACO: 4.5.2,IIA 5.6.10
3161345	2016, SYN546330 - Oral (Gavage) Preliminary Prenatal Developmental Toxicity Study in the Rabbit, DACO: 4.5.3,IIA 5.6.11
3161346	2017, SYN546330 - Oral (Gavage) Prenatal Developmental Toxicity Study in the Rabbit, DACO: 4.5.3,IIA 5.6.11
3161348	2019, SYN546330 - Oral (Gavage) Tolerability Study in the Non-Pregnant Rabbit, DACO: 4.5.3,IIA 5.6.11
3161350	2020, Supplemental Data to Support SYN546330 - Oral (Gavage) Prenatal Developmental Toxicity Study in the Rabbit, DACO: 4.5.3,IIA 5.6.11
3161351	2018, SYN546330 - Neurotoxicity Study by a Single Oral Gavage Administration to Han Wistar Rats followed by a 14-Day Observation Period, DACO: 4.5.12,IIA 5.7.1
3161352	2020, Supplemental Data to Support SYN546330 - Neurotoxicity Study by a Single Oral Gavage Administration to Han Wistar Rats followed by a 14-Day Observation Period, DACO: 4.5.12,IIA 5.7.1
3161354	2020, Spiropidion - Waiver Request for a Subchronic Neurotoxicity Study in Rats, DACO: 4.5.13,IIA 5.7.4
3436631	2022, Syngenta Comments on the PMRA Toxicology Evaluation of Spiropidion in the IT-MRL Submission (2020-4760) and Position on a Potential Common Mechanism of Toxicity with Other Insecticides of the Same Mode of Action, DACO: 4.1,IIA 5.11
3436632	2022, Spiropidion - Assessment to Waive Requirement for Repeat Dose Inhalation Study, DACO: 4.3.6,IIA 5.3.6
3436633	2022, Short-term Repeated Dose 28-day Inhalation Toxicity Study of Spiropidion (SYN546330) in Rats (Pretest 5-day Tolerability Study), DACO: 4.3.6,IIA 5.3.6
3436634	2020, SYN546330 - Assessment of Airway Irritation Potential of a Pesticide Formulation In Vitro Using the MucilAir Airway Model, DACO: 4.3.6,IIA 5.3.6

3436635	2022, SYN546330 - Single Exposure Inhalation Study with Pharmacokinetics in Wistar Han Rats, DACO: 4.3.6,IIA 5.3.6
3436636	2020, SYN549098 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay, DACO: 4.5.4,IIA 5.4.1
3436637	2020, SYN549098 - Micronucleus Test in Human Lymphocytes In Vitro, DACO: 4.5.6,IIA 5.4.2
3436638	2022, SYN549098 - Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT), DACO: 4.5.5,IIA 5.4.3
3436640	2022, Spiropidion - Technical Position on the OECD 414 Prenatal Developmental Toxicity Study in the Rat and Rabbit, DACO: 4.5.2,4.5.3,IIA 5.6.10,IIA 5.6.11
3740600	2022, SYN546330 tech. - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay, DACO: 4.5.4
3740601	2018, SYN550827 - Salmonella Typhimurium and Escherichia Coli Reverse Mutation Assay, DACO: 4.5.4
3740602	2022, SYN546330 tech. - Gene Mutation Assay in Chinese Hamster V79 Cells In Vitro (V79/HPRT), DACO: 4.5.5
3740603	2018, SYN550827 - Micronucleus Test in Human Lymphocytes In Vitro, DACO: 4.5.6
3436645	2022, SYN546330 - Metabolism of [14C]-SYN546330 in Potatoes, DACO: 6.3,IIA 6.2.1
3436596	2021, Validation of Analytical Method GRM069.08A for the Determination of SYN546330 and its Metabolites SYN547305, SYN548430, SYN550821, SYN549937, SYN548033, and SYN550838 in Rotational Crops, DACO: 7.2.1,7.2.4,IIA 4.3
3436599	2021, SYN546330 - Analytical Method GRM069.10A for the Determination of the Metabolite SYN549098 in Rotational Crops, DACO: 7.2.1,7.2.4,IIA 4.3
3436600	2022, SYN546330 - Analytical Method GRM069.12A Validation of SYN546330 and its Metabolites SYN547305, SYN547435, and SYN548430 in Oil, DACO: 7.2.1,7.2.4,IIA 4.3
3436603	2020, SYN546330 - Validation of Syngenta Method, based upon GRM069.18A, for the Determination of Residues of SYN550735 in Apples and Oranges by LC-MS/MS, DACO: 7.2.1,7.2.4,IIA 4.3
3436604	2022, SYN546330 - Analytical Method GRM069.12A for the Determination of SYN546330 and its Metabolites SYN547305, SYN547435, SYN548430, SYN550820 and SYN550839 in Oil, DACO: 7.2.1,7.2.4,IIA 4.3
3436605	2021, SYN546330 - Analytical Method GRM069.08A for the Determination of SYN546330 and its Metabolites SYN547305, SYN548430, SYN550821, SYN549937, SYN548033 and SYN550838 in Rotational Crops by LC-MS/MS Direct Injection Analysis, DACO: 7.2.1,7.2.4,IIA 4.3

3436606	2021, Validation of Analytical Method GRM069.10A for the Determination of SYN546330 Metabolite SYN549098 in Rotational Crops, DACO: 7.2.1,7.2.4,IIA 4.3
3436641	2022, Two Year Frozen Storage Stability of SYN550839 and SYN550735 in Processed Crop Fractions, DACO: 7.3,IIA 6.1.1
3436643	2021, SYN546330 - Storage Stability of Residue of Metabolites SYN550820 and SYN550839 in Crop Matrices Stored Frozen for up to Two Years, and SYN550735 in Oranges and Apples Stored for up to 18 Months and Two Years (Replaces MRID 51174647), DACO: 7.3,IIA 6.1.1
3436644	2022, Frozen Storage Stability of SYN546330, SYN547305, SYN548430, SYN550821, SYN549937, SYN548033, SYN550838, and SYN549098 in Rotational Crops, DACO: 7.3,IIA 6.1.2
3436649	2022, Spiropidion (A20262B) - Magnitude of the Residues in and on Cotton Raw Agricultural Commodities USA 2020, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436650	2022, Spiropidion SC (A20262B) - Magnitude of the Residues in Grapes - USA 2021, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436651	2022, Spiropidion (A20262B) - Magnitude of the Residues in and on Raw Agricultural Commodities of Brassica Head and Stem Vegetables (CG 5-16), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436652	2022, Spiropidion SC (A20262B) - Magnitude of the Residues in Apples and Pears as Representative Crops for The Pome Fruit Crop Group (EPA 11-10, PMRA CG11-09), USA 2021, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436653	2022, NA11630 - Magnitude of the Residue on Cucumber (Greenhouse), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436654	2022, Spiropidion (A20262B) - Magnitude of the Residues in and on Leafy Vegetable Raw Agricultural Commodities USA 2020, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436655	2022, NA-11630: Magnitude of the Residue on Pepper, Greenhouse, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436656	2022, NA-11630: Magnitude of the Residue on Tomato, Greenhouse, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436647	2019, SYN546330 SC (A20262B) - Magnitude of the Residue in or on Orange, Grapefruit, and Lemon as Representative Commodities of Citrus Fruit, Group 10, and Processed Fractions, USA 2017 and 2018, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436648	2019, SYN546330 (A20262B) - Magnitude of the Residues in Cotton, USA, 2017, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
3436657	2022, SYN546330 SC (A20262B) - Magnitude of the Residues in or on Apple Processed Commodities - USA 2020, DACO: 7.4.5,IIA 6.5.3
3436658	2022, SYN546330 SC (A20262B) - Magnitude of the Residues in or on Grape Processed Commodities - USA 2020, DACO: 7.4.5,IIA 6.5.3
3436659	2019, SYN546330 - Uptake and Metabolism of [14C]-SYN546330 in Confined Rotational Crops, DACO: 7.4.4,IIA 6.6.2

3436661	2022, SYN546330 - Confirmation of SYN552982 in Selected Samples from Confined Rotational Crop Study TK0136983, DACO: 7.4.4,IIA 6.6.2
3436663	2022, Spiropidion: The Rationale for not including SYN552982 as an Analytical Target in the Limited Rotational Crop Residue Studies, DACO: 7.4.4,IIA 6.6.3,IIA 6.8.7
3436665	2022, Spiropidion - The Rationale for not including a Tentatively Identified Metabolite (Unknown 4) as an Analytical Target in the Limited Rotational Crop Residue Studies, DACO: 7.4.4,IIA 6.6.3,IIA 6.8.7
3436667	2022, SYN546330 SC (A20262B) - Field Accumulation in Rotational Crops (30-, 90-, 180- and 270-day Plant Back Intervals) USA 2020, DACO: 7.4.4,IIA 6.6.3,IIA 6.8.7
3161381	2019, SYN548430 - Aqueous Hydrolysis of [14C]-SYN548430 at 90°C, 100°C and 120°C, DACO: 7.4.5,IIA 6.5.1
3161382	2016, SYN546330 - High Temperature Hydrolysis of [14C] SYN546330 at 90°C, 100°C and 120°C, DACO: 7.4.5,IIA 6.5.1
3161383	2018, SYN547305 - High Temperature Hydrolysis of [14C]-SYN547305 at 90, 100 and 120°C, DACO: 7.4.5,IIA 6.5.1
3161384	2019, SYN547435 - Aqueous Hydrolysis of [14C]-SYN547435 at 90°C, 100°C and 120°C, DACO: 7.4.5,IIA 6.5.1

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PMRA Document Number	Reference
3492193	2023, Physicochemical Properties of the Spiropidion Transformation Products (Metabolites) SYN547305, SYN548430, SYN548274, SYN552045, SYN548037, SYN552257 and 1-methoxy-4-[methyl (oxalo) amino] piperidine-4-carboxylic acid (SYN551480), DACO: 8.2.1 CBI
3492194	2023, Hydrolysis of the Spiropidion Transformation Product (Metabolite) SYN547305 - Waiver Rationale, DACO: 8.2.3.2
3498956	2023, Confidential Business Information Removed - Physicochemical Properties of the Spiropidion Transformation Products (Metabolites) SYN547305, SYN548430, SYN548274, SYN552045, SYN548037, SYN552257 and 1-methoxy-4-[methyl (oxalo) amino] piperidine-4-carboxylic acid (SYN551480), DACO: 8.2.1 CBI
3498957	2023, Physicochemical Properties of the Spiropidion Transformation Products (Metabolites) SYN547305, SYN548430, SYN548274, SYN552045, SYN548037, SYN552257 and 1-methoxy-4-[methyl (oxalo) amino] piperidine-4-carboxylic acid (SYN551480), DACO: 8.2.1
3436669	2018, SYN546330 - Aerobic Soil Metabolism of [14C]-SYN546330, DACO: 8.2.3.4.2,IIA 7.1.1
3436671	2018, SYN546330 - Anaerobic Soil Metabolism of [14C]-SYN546330, DACO: 8.2.3.4.4,IIA 7.1.2
3436672	2018, SYN546330 - Soil Photolysis of [14C]-SYN546330, DACO: 8.2.3.3.1,IIA 7.1.3

3436676	2018, SYN547305 - Further Extraction and Analysis of Samples Generated under an Aerobic Soil Rate of Degradation Study (TK0213972), DACO: 8.2.3.4.2,IIA 7.2.3
3436677	2017, SYN547305 - Rate of Degradation of [14C]-SYN547305, DACO: 8.2.3.4.2,IIA 7.2.3
3436678	2021, SYN548033 - Rate of Degradation of 14C-SYN548033 in Soils at 20ºC, DACO: 8.2.3.4.2,IIA 7.2.3
3436679	2019, SYN548037 - Rate of Degradation of 14C-SYN548037 in Soils at 20ºC, DACO: 8.2.3.4.2,IIA 7.2.3
3436680	2022, SYN549098 - Rate of Degradation of 14C-SYN549098 in Soils at 20ºC, DACO: 8.2.3.4.2,IIA 7.2.3
3436683	2022, SYN552045 - Rate of Degradation of SYN552045 in Aerobic Soils at 20ºC, DACO: 8.2.3.4.2,IIA 7.2.3
3436684	2022, SYN552257 - Rate of Degradation of [14C]-SYN552257 in Soils at 20ºC, DACO: 8.2.3.4.2,IIA 7.2.3
3436686	2022, SYN546330 SC (A20262B) - Dissipation of the Insecticide SYN546330 in Soil When Applied at a Typical Early Season Application Timing for Pome Fruit in the Finger Lakes Region of New York, USA, DACO: 8.3.2,IIA 7.3.1
3436694	2021, Freezer Stability of SYN546330 and Its Degradation Products In Turfgrass Clippings, Thatch-Sod, and Soil Matrices from California, Iowa, and New York Terrestrial Field Dissipation Studies, DACO: 8.3.2,IIA 7.3.1
3436696	2022, SYN546330 - Dissipation Trial to Determine Persistence and Leaching Movement of SYN546330 and any Significant Soil Degradates in Soil, DACO: 8.3.2,IIA 7.3.1
3436698	2018, SYN546330 - Adsorption Properties of [14C]-SYN546330 in OECD Type 2 and Type 4 Soils, DACO: 8.2.4.2,IIA 7.4.1
3436699	2018, SYN546330 - Adsorption/Desorption of [14C]-SYN546330, DACO: 8.2.4.2,IIA 7.1.2,IIA 7.4.1
3436700	2021, SYN547305 - Adsorption/Desorption Properties of 14C-SYN547305 in Two Alkaline Soils, DACO: 8.2.4.2,IIA 7.4.2
3436701	2017, SYN547305 - Adsorption/Desorption Properties of 14C-SYN547305, DACO: 8.2.4.2,IIA 7.4.2
3436702	2018, SYN547305 - Adsorption Properties of [^{14}C]-SYN547305 in OECD Type 2 and Type 4 Soils, DACO: 8.2.4.2,IIA 7.4.2
3436703	2021, SYN548033 - Adsorption and Desorption of [^{14}C]-SYN548033, DACO: 8.2.4.2,IIA 7.4.2
3436704	2019, SYN548037 - Adsorption and Desorption of [^{14}C]-SYN548037, DACO: 8.2.4.2,IIA 7.4.2
3436708	2022, SYN552045 - Adsorption and Desorption of [^{14}C]-SYN552045 in Three Soils, DACO: 8.2.4.2,IIA 7.4.2
3436709	2022, SYN552257 - Adsorption and Desorption of ^{14}C-SYN552257 in Three Soils, DACO: 8.2.4.2,IIA 7.4.2
3436710	2018, SYN546330 - Hydrolysis of [^{14}C]-SYN546330, DACO: 8.2.3.2,IIA 7.5
3436711	2018, SYN546330 - Aqueous Photolysis of [^{14}C]-SYN546330, DACO: 8.2.3.3.2,IIA 7.6
3436712	2017, SYN546330 - Anaerobic Aquatic Sediment Metabolism of [^{14}C]-SYN546330, DACO: 8.2.3.5.6,IIA 7.8.3

3436713	2017, SYN546330 - Aerobic Aquatic Sediment Metabolism of [^{14}C]-SYN546330, DACO: 8.2.3.5.4,IIA 7.8.3
3436714	2016, SYN546330 - 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
3436715	2018, SYN546330 - An Acute Oral Toxicity Study with the Mallard using a Sequential Testing Procedure, DACO: 9.6.2.2,IIA 8.1.1
3436716	2022, SYN546330 - A Dietary LC_{50} Study with the Mallard, DACO: 9.6.2.5,IIA 8.1.2
3436717	2022, SYN546330 - A Dietary LC_{50} Study with the Northern Bobwhite, DACO: 9.6.2.4,IIA 8.1.2
3436718	2022, SYN546330 - A Dietary LC_{50} Study with the Zebra Finch, DACO: 9.6.2.6,IIA 8.1.3
3436719	2022, SYN546330 - A Reproduction Study with the Northern Bobwhite, DACO: 9.6.3.1,IIA 8.1.4
3436720	2022, SYN546330 - A Reproduction Study with the Mallard, DACO: 9.6.3.2,IIA 8.1.4
3436723	2018, SYN546330 - A 96-Hour Shell Deposition Test with the Eastern Oyster (*Crassostrea virginica*), DACO: 9.4.4,IIA 8.11.1
3436724	2018, SYN546330 - A 96-Hour Flow-Through Acute Toxicity Test with the Saltwater Mysid (*Americamysis bahia*), DACO: 9.4.2,IIA 8.11.1
3436725	2018, SYN546330 - A 96-Hour Flow-Through Acute Toxicity Test with the Sheepshead Minnow (*Cyprinodon variegatus*), DACO: 9.5.2.4,IIA 8.11.1
3436726	2022, SYN546330 - A Flow-Through Life-Cycle Toxicity Test with the Saltwater Mysid (*Americamysis bahia*), DACO: 9.4.5,IIA 8.11.2
3436727	2022, SYN546330 - An Early Life-Stage Toxicity Test with the Sheepshead Minnow (*Cyprinodon variegatus*), DACO: 9.5.3.1,IIA 8.11.2
3436728	2020, Spiropidion SC (A20262B) plus Citrol-ina (EC) - Evaluation of the Phytotoxicity to Non Target Terrestrial Plant Vegetative Vigour Test, DACO: 9.8.4,IIA 8.12
3436729	2020, Spiropidion SC (A20262B) plus Citrol-ina (EC) - Evaluation of the Phytotoxicity to Non Target Terrestrial Plant Seedling Emergence and Seedling Growth Test, DACO: 9.8.4,IIA 8.12
3436732	2019, SYN546330 (A20262B) - Determination of Residues in Leaves, Flowers, Pollen, and Nectar of Cucumber after Foliar Application, DACO: 9.2.4.8,IIA 8.16.2
3436734	2019, Magnitude of residues of SYN546330 and its metabolite SYN547305 in soil, leaves, flowers, anthers and nectar of dry bean after foliar applications of A20262, DACO: 9.2.4.8,IIA 8.16.2
3436736	2017, SYN546330 - Residue Study on Cucumber Pollen and Nectar in Northern France, Germany, Spain and Italy in 2015, DACO: 9.2.4.8,IIA 8.16.2
3436737	2021, SYN546330 SC (A20262B) - Determination of Residues in Leaves, Flowers, Pollen, and Nectar of Pome (Apple) After Foliar Applications, DACO: 9.2.4.8,IIA 8.16.2
3436739	2019, Magnitude of Residues of SYN546330 and its Metabolite SYN547305 in Environmental Matrices of Tomato Plants and in Soil after Foliar Application with A20262 and A21781, DACO: 9.2.4.8,IIA 8.16.2

3436741	2019, Magnitude of residues of SYN546330 and its metabolite SYN547305 in soil, leaves, flowers and anthers of potato after foliar applications with A21781., DACO: 9.2.4.8,IIA 8.16.2
3436744	2018, SYN546330 - A 96-Hour Flow-Through Acute Toxicity Test with the Rainbow Trout (*Oncorhynchus mykiss*), DACO: 9.5.2.1,IIA 8.2.1.1
3436746	2018, SYN547305 - A 96-Hour Static Acute Toxicity Test with the Rainbow Trout (*Oncorhynchus mykiss*), DACO: 9.5.2.1,IIA 8.2.1.1
3436748	2018, SYN546330 - A 96-Hour Flow-Through Acute Toxicity Test with the Common Carp (*Cyprinus carpio*), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
3436750	2018, SYN546330 - A 96-Hour Flow-Through Acute Toxicity Test with the Fathead Minnow (*Pimephales promelas*), DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
3436752	2018, SYN546330 - An Early Life-Stage Toxicity Test with the Fathead Minnow (*Pimephales promelas*), DACO: 9.5.3.1,IIA 8.2.4
3436753	2018, SYN546330 - An Aqueous Exposure Bioaccumulation Test with the Bluegill (*Lepomis macrochirus*), DACO: 9.5.6,IIA 8.2.6.1
3436754	2017, SYN546330 - Acute Toxicity to *Daphnia magna* in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1
3436755	2018, SYN547305 - Acute Toxicity to *Daphnia magna* in a 48-Hour Immobilization Test, DACO: 9.3.2,IIA 8.3.1.1
3436756	2018, SYN546330 - A 48-Hour Static Renewal Acute Toxicity Test with the Midge (*Chironomus riparius*), DACO: 9.3.4,IIA 8.3.1.2
3436757	2018, SYN547305 - A 48-Hour Static Acute Toxicity Test with the Midge (*Chironomus riparius*), DACO: 9.3.4,IIA 8.3.1.2
3436758	2021, SYN548033 - Effects on First-Instar Larvae of *Chironomus riparius* in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2
3436759	2021, SYN548274 - Effects on First-Instar Larvae of *Chironomus riparius* in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2
3436760	2021, SYN548430 - Effects on First-Instar Larvae of *Chironomus riparius* in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2
3436763	2021, SYN551480 - Effects on First-Instar Larvae of *Chironomus riparius* in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2
3436764	2021, SYN552045 - Effects on First-Instar Larvae of *Chironomus riparius* in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2
3436765	2021, SYN552257 - Effects on First-Instar Larvae of *Chironomus riparius* in a 48-Hour Immobilization Test, DACO: 9.3.4,IIA 8.3.1.2
3436766	2018, SYN546330 - A Flow-Through Life-Cycle Toxicity Test with the Cladoceran (*Daphnia magna*), DACO: 9.3.3,IIA 8.3.2.1
3436767	2018, SYN546330 - A 96-Hour Toxicity Test with the Cyanobacteria (*Anabaena flos-aquae*), DACO: 9.8.2,IIA 8.4
3436768	2018, SYN546330 - A 96-Hour Toxicity Test with the Freshwater Diatom (*Navicula pelliculosa*), DACO: 9.8.2,IIA 8.4
3436769	2018, SYN546330 - A 96-Hour Toxicity Test with the Freshwater Alga (*Raphidocelis subcapitata*), DACO: 9.8.2,IIA 8.4
3436770	2018, SYN546330 - A 96-Hour Toxicity Test with the Marine Diatom (*Skeletonema costatum*), DACO: 9.8.2,IIA 8.4
3436771	2018, SYN547305 - Toxicity to *Pseudokirchneriella subcapitata* in a 96 Hour Algal Growth Inhibition Test, DACO: 9.8.2,IIA 8.4

3436773	2022, SYN546330 - A 10-Day Toxicity Test with the Freshwater Amphipod (*Hyalella azteca*) Using Spiked Whole Sediment, DACO: 9.3.4,IIA 8.5.1
3436774	2022, SYN546330 - A 10-Day Toxicity Test with the Marine Amphipod (*Leptocheirus plumulosus*) Using Spiked Whole Sediment, DACO: 9.3.4,IIA 8.5.1
3436775	2022, SYN546330 - A 10-Day Toxicity Test with the Midge (*Chironomus dilutus*) Using Spiked Whole Sediment, DACO: 9.3.4,IIA 8.5.1
3436776	2018, SYN546330 - Toxicity to the Aquatic Higher Plant *Lemna gibba* in a 7-day Growth Inhibition Test, DACO: 9.8.5,IIA 8.6
3436777	2015, SYN546330 - Chronic toxicity to the honeybee *Apis mellifera* L. in a 10 day continuous laboratory feeding study, DACO: 9.2.4.4,IIA 8.7.1
3436778	2018, SYN546330 - Acute toxicity to the honeybee *Apis mellifera* L. under laboratory conditions, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1
3436779	2018, SYN546330 - Acute Toxicity to the Bumblebee *Bombus terrestris* L. under Laboratory Conditions, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1
3436780	2018, SYN547305 - Chronic toxicity to the honey bee *Apis mellifera* L. in a 10 day continuous laboratory feeding study, DACO: 9.2.4.4,IIA 8.7.1
3436781	2018, SYN547305 - Acute toxicity to the honeybee *Apis mellifera* L. under laboratory conditions, DACO: 9.2.4.2,IIA 8.7.1
3436782	2017, SYN546330 SC (A20262B) - A Semi-Field Study to Evaluate Effects on Honeybees (Apis mellifera L.) after Two Applications in *Phacelia tanacetifolia* in Germany 2016, DACO: 9.2.4.6,IIA 8.7.4
3436783	2019, SYN546330 (A20262B) and its Metabolite SYN547305 - Effects on Honeybee (*Apis mellifera* L.) Adults and Brood in Semi-Field Test Conditions, DACO: 9.2.4.3,IIA 8.7.4
3436784	2016, SYN546330 - Effects on the Honeybee Brood *Apis mellifera* L. Following Single Oral Exposure Under Field Conditions, DACO: 9.2.4.7,IIA 8.7.4
3436785	2018, SYN546330 - Repeated Exposure to the Honey Bee (*Apis mellifera*) Larvae under Laboratory Conditions (until Adult Emergence at Day 22), DACO: 9.2.4.3,IIA 8.7.4
3436786	2018, SYN546330 - Single Exposure to the Honey Bee (*Apis mellifera*) Larvae under Laboratory Conditions, DACO: 9.2.4.3,IIA 8.7.4
3436787	2022, SYN546330 technical - Honey Bee Brood and Colony Level Effects Following SYN546330 Exposure via Treated Sucrose Solution in a Field Study in North Carolina - USA in 2021-2022, DACO: 9.2.4.7,IIA 8.7.4
3436788	2018, SYN547305 - Repeated Exposure to the Honey Bee (*Apis mellifera*) Larvae under Laboratory Conditions (until Adult Emergence at Day 22), DACO: 9.2.4.3,IIA 8.7.4
3436789	2018, SYN547305 - Single Exposure to the Honey Bee (*Apis mellifera*) Larvae under Laboratory Conditions (in vitro), DACO: 9.2.4.3,IIA 8.7.4
3436790	2017, SYN546330 SC (A20262B) - A laboratory bioassay of the effects of fresh residues on the parasitic wasp *Aphidius rhopalosiphi* (Hymenoptera, Braconidae), DACO: 9.2.6,IIA 8.8.1.1
3436791	2020, Acute Toxicity Test to *Trichogramma* with Spiropidion TC, DACO: 9.2.6,IIA 8.8.1.1

3436792	2017, SYN546330 SC (A20262B) - A rate-response laboratory bioassay of the effects of fresh residues on the predatory mite *Typhlodromus pyri* (Acari: Phytoseiidae), DACO: 9.2.5,IIA 8.8.1.2
3436794	2017, SYN546330 SC (A20262B) - Effects on the Reproduction of the Collembolan *Folsomia candida*, DACO: 9.2.5,IIA 8.8.1.3
3436796	2018, SYN547305 - Effects on the Reproduction of the Collembolan *Folsomia candida*, DACO: 9.2.5,IIA 8.8.1.3
3436798	2017, SYN546330 SC (A20262B) - Effects on the Reproduction of the Predatory Mite *Hypoaspis aculeifer*, DACO: 9.2.5,IIA 8.8.2.3
3436800	2018, SYN547305 - Effects on the Reproduction of the Predatory Mite *Hypoaspis aculeifer*, DACO: 9.2.5,IIA 8.8.2.3
3436803	2020, Natural Enemy (Ladybird beetles) Acute Contact Toxicity Test with Spiropidion TC, DACO: 9.2.7,IIA 8.8.2.5
3436805	2020, Acute Toxicity Test to Silkworm with Spiropidion TC, DACO: 9.2.7,IIA 8.8.2.5
3436806	2016, SYN546330 - Acute Toxicity to the Earthworm *Eisenia fetida* in Artificial Soil, DACO: 9.2.3.1,IIA 8.9.1
3436809	2017, SYN547305 - Acute Toxicity to the Earthworm *Eisenia Andrei* in Artificial Soil, DACO: 9.2.3.1,IIA 8.9.1
3436811	2017, SYN546330 SC (A20262B) - Sublethal Toxicity to the Earthworm *Eisenia andrei* in Artificial Soil with 5 % Peat, DACO: 9.2.3.2,IIA 8.9.2
3436812	2018, SYN547305 - Sublethal Effects on the Reproduction of the Earthworm *Eisenia andrei* in Artificial Soil with 5 % Peat, DACO: 9.2.3.1,IIA 8.9.2
3436814	2020, SYN548033 - Sublethal Effects on the Reproduction of the Earthworm *Eisenia andrei* in Artificial Soil with 5 % Peat, DACO: 9.2.3.2,IIA 8.9.2
3436817	2021, SYN552045 - Sublethal Effects on the Reproduction of the Earthworm *Eisenia andrei* in Artificial Soil with 10 % Peat, DACO: 9.2.3.2,IIA 8.9.2
3436818	2021, SYN552257 - Sublethal Effects on the Reproduction of the Earthworm *Eisenia andrei* in Artificial Soil with 10 % Peat, DACO: 9.2.3.2,IIA 8.9.2
3436483	2018, SYN546330 - The In Vivo Percutaneous Absorption of Radiolabelled SYN546330 in Concentrate Formulation and Three In-Use Dilutions in the Rat, DACO: 5.8,IIIA 7.6.1.
3436485	2018, SYN546330 SC (A20262B) - The In Vitro Percutaneous Absorption of Radiolabelled SYN546330 in Concentrate Formulation and Three In-Use Dilutions through Human Split-Thickness Skin, DACO: 5.8,IIIA 7.6.2.
3436484	2019, SYN546330 SC (A20262B) - The In Vitro Percutaneous Absorption of Radiolabelled SYN546330 in Concentrate Formulation and Three In-Use Dilutions Through Rat Split-Thickness Skin, DACO: 5.8,IIIA 7.6.2
3465137	2023, SYN546330 Technical - Honey Bee Brood and Colony Level Effects Following SYN546330 Exposure via Treated Sucrose Solution in a Field Study in North Carolina - USA in 2021-2022 (Replaces MRID 51814447), DACO: 9.2.4.3
3465138	2023, SYN546330 Technical - Honey Bee Brood and Colony Level Effects Following SYN546330 Exposure via Treated Sucrose Solution in a Field Study in North Carolina - USA in 2021-2022, DACO: 9.2.4.3

3524458	2023, SYN546330 (A20262B) and its Metabolite SYN547305: Effects on Honeybee (Apis mellifera L.) Adults and Brood in Semi-Field Test Conditions (Replaces MRID 51814449) - Amendment 3, DACO: 9.2.4.3
3657446	US EPA, 2014, US EPA, Memorandum: Toxicity Testing and Ecological Risk Assessment Guidance for Benthic Invertebrates, DACO: 9.9

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PMRA No. References	
3436366	2022, A20262A/B - Document MIII, Section 7 - Efficacy Data and Information - Canada, DACO: 1.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.2, 10.2.3.3, 10.2.3.4, 10.3.1, 10.3.2, 10.4,10.5.1, 10.5.2, 10.5.4,10.6,12.7, Document M,IIIA 1.6,IIIA 3.1,IIIA 3.2,IIIA 3.3.1,IIIA 3.3.2,IIIA 3.3.3,IIIA 3.4,IIIA 3.5,IIIA 3.6,IIIA 3.7.1,IIIA 3.9,IIIA 6.1.2,IIIA 6.1.3,IIIA 6.2.1,IIIA 6.2.2,IIIA 6.2.3,IIIA 6.3,IIIA 6.4.1,IIIA 6.4.2,IIIA 6.4.3,IIIA 6.5,IIIA 6.6
3436381	2016, 2016 Trial Insecticides on Greenhouse Peppers for Control of Twospotted Spider Mites, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436382	2017, Efficacy of Product A for the Control of Twospotted Spider Mites on Greenhouse Tomatoes, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436383	2017, Efficacy of Product A for the Control of Twospotted Spider Mites on Greenhouse Tomatoes, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436384	2015, Cyflumetofen on Greenhouse Peppers vs Twospotted Spider Mites (TSSM), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436385	2019, Evaluation of Insecticide Treatments in Greenhouse Cucumbers, DACO: 1
3436386	2021, Performance of NA11630 (A20262 Insecticide) on Greenhouse Grown Eggplant, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436387	2022, Performance of Spiropidion on Greenhouse Grown Eggplant Against Piercing Sucking Insects, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436388	2016, Efficacy for the Management of Twospotted Spider Mite (Tetranychus urticae) and Tolerance of Greenhouse Cucumber in the Fraser Valley, British Columbia (Zone 12), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436389	2022, To Determine the Efficacy of and Crop Tolerance to NA-11630 (A20262 Insecticide) on Greenhouse Peppers, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436390	2022, A20262 Insecticide - Aphids -Tank-mix Adjuvants, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436391	2016, A20262 Insecticide_SC300: Bemisia on tomato RS317A, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436392	2016, A20262 Insecticide_SC300: Bemisia on tomato RS317A, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436393	2018, Avaliação do risco de fitotoxidez de Ochima em mistura com Star 300 SC e Star + Aceta na cultura do Tomate (Caracterização), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436394	2019, Registro de Elestal (A20262) em aplicao em Bandeja, Drench e Bandeja+Drench para controle de Bemisia tabaci em tomate (LAUDO), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3436395	2016, A20262 Insecticide SC300: Bemisia on tomato RS317A, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436396	2015, A20262 Insecticide - Dysaphis plantaginea on Apples - Defining 300SC Dose and Mixture Benefits, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436397	2015, A20262 Insecticide Stage 3 EAME CP Efficacy Trials 2015 - Aphis pomi on Apple, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436398	2018, A20262 Insecticide - Test Possible Backups for Acetamiprid, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436400	2019, Technical Benefits of Spiropidion on Residuality and Plant Mobility/ Semi field (Lower canopy sprayed leaves), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436402	2019, Technical Benefits of Spiropidion on Residuality and Plant Mobility/ Semi Field (Upper canopy - Unsprayed leaves), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436405	2019, Technical Benefits of Spiropidion on Residuality and Plant Mobility/ Semi Field (Lower canopy - sprayed leaves), DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436407	2018, Registration Trials of A19526X (Spiropidion 100 SC) Against Aphids in Tomato (flowering/post flowering) in Greenhouse, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436409	2014, A20262 Insecticide - Whiteflies on Vegetables (no brassica) - Built-in Formulations, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436411	2014, A20262 Insecticide - Aphids on Fruiting Vegetables and Cucurbits (no brassica) - Built-in Formulations, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436413	2013, A20262 Insecticide - Tetranychus urticae on Vegetables, Legumes and Strawberries - Built-in Formulations, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436415	2018, Registration Trials of A19526X (Spiropidion 100 SC) Against Aphis gossypii in Melon (flowering/post flowering) in Greenhouse, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436417	2015, A20262 Insecticide Stage 3 EAME CP Efficacy Trials 2015 Mites on Veggies, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436418	2019, Registration Trials of A19526X (Spiropidion 100 SC) Against M. persicae Post-Flowering Application for Efficacy Evaluation on Pepper in OF, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436419	2019, GEP- registration trials of A19526X (Spiropidion 100 SC) against M. persicae flowering/postflowering application, for efficacy evaluation on melon in OF, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436420	2018, GEP registration trials of A19526X (Spiropidion 100 SC) against Bemisia tabaci in zucchini in GH, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436421	2014, 2_A20262 Insecticide: Aphids on fruiting vegetables and cucurbits (no brassica) - built-in formulations, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436422	2019, GEP- registration trials of A19526X (Spiropidion 100 SC) against M. persicae post-flowering application, for efficacy evaluation on pepper in OF, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3436424	2019, GEP- registration trials of A19526X (Spiropidion 100 SC) against M. persicae post-flowering application, for efficacy evaluation on pepper in OF, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436425	2018, GEP Registration trials of A19526X (Spiropidion 100 SC) against aphids in tomato (flowering/post flowering) in GH, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436426	2017, tomato efficacy against whiteflies_1st Wave_APAC A20262 Insecticide_SC100 in-house efficacy trials 2017_Solanaceae, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436427	2014, 2_A20262 Insecticide_SYN547407: Thrips on vegetables - Mix ABAM, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436428	2017, A20262 Insecticide_ACET benefits of ready mix over solo products against aphids and WF on vegetables in greenhouse, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436429	2016, DEVELOP A20262 Insecticide 100 SC IN TOMATO IN TURKEY AGAINST TETRANYCHUS URTICAE IN GH, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436430	2019, NA-11630: US Efficacy Trials - Aphid in Fruiting Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436431	2019, NA-11630: US Efficacy Trials - Aphid in Cucurbit Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436432	2020, NA-11630: US Efficacy Trials - Aphid in Fruiting Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436433	2020, NA-11630: US Efficacy Trials - Aphid in Cucurbit Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436434	2021, ISM-555 CP US 2021 SC200 profiling - thrips in vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436435	2021, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436436	2021, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436437	2021, NA-11630: US Efficacy Trials - Aphids in apples, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436438	2020, NA-11630: US Efficacy Trials - Aphids in apples, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436439	2021, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436440	2020, NA-11630: US Efficacy Trials - Whitefly in Fruiting Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436441	2020, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436442	2021, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436443	2020, NA-11630: US Efficacy Trials - Whitefly in Cucurbit Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436444	2021, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3436445	2021, NA-11630: US Efficacy Trials - Whitefly in Cucurbit Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436446	2020, NA-11630: US Efficacy Trials - Whitefly in Cucurbit Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436447	2019, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436448	2019, NA-11630: US Efficacy Trials - Whitefly in Cucurbit Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436449	2020, NA-11630: US Efficacy Trials - Aphid in Leafy Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436450	2020, NA-11630: US Efficacy Trials - Whitefly in Cucurbit Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436451	2019, NA-11630: US Efficacy Trials - Aphid in Leafy Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436452	2019, NA-11630: US Efficacy Trials - Aphid in Brassica Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436453	2019, NA-11630: US Efficacy Trials - Aphid in Leafy Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436454	2022, NA-11630: US Efficacy Trials - Mealybugs in grapes, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436455	2020, NA-11630: US Efficacy Trials - Aphid in Leafy Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436456	2020, NA-11630: US Efficacy Trials - Mealybugs in grapes, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436457	2019, NA-11630: US Efficacy Trials - Aphid in Cucurbit Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436458	2020, NA-11630: US Efficacy Trials - Aphid in Cucurbit Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436459	2021, NA-11630: US Efficacy Trials - Aphid in Cucurbit Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436460	2021, NA-11630: US Efficacy Trials - Mealybugs in grapes, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436461	2020, NA-11630: US Efficacy Trials - Whitefly in Fruiting Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436462	2021, NA-11630: US Efficacy Trials - Whitefly in Fruiting Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436463	2019, NA-11630: US Efficacy Trials - Whitefly in Fruiting Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436464	2020, NA-11630: US Efficacy Trials - Aphid in Fruiting Vegetable, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436465	2020, NA-11630: US Efficacy Trials - Whitefly in Fruiting Vegetables, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436466	2021, NA-11630: US Efficacy Trials - Mealybugs in grapes, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436467	2020, NA-11630: US Efficacy Trials - Aphids in apples, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3

3436468	2019, A20262 Insecticide_SC300 foliar for white fly control on tomato, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436469	2017, A20262 Insecticide Profiling against White Fly on Cucumber in Vietnam, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436470	2020, A20262 Insecticide_SC300 foliar for white fly control on tomato, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436471	2018, A20262 Insecticide: Efficacy of White fly control on eggplant in Vietnam 2018, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436472	2018, A20262 Insecticide: Efficacy of White fly control on cucumber in Vietnam 2018, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436473	2018, A20262 Insecticide: Efficacy of White fly control on eggplant in Vietnam 2018, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436474	2017, A20262 Insecticide Profiling against White Fly on Cucumber in Vietnam, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3
3436475	2015, 3_A20262 Insecticide: Whiteflies and aphids - tank-mix adjuvants, DACO: 10.2.3.3,10.2.3.4,IIIA 6.1.2,IIIA 6.1.3