Proposed Registration Decision PRD2025-07

Fluoxapiprolin and Xivana Prime

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Overview

Proposed Registration Decision for Fluoxapiprolin

Health Canada's Pest Management Regulatory Agency (PMRA), pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Fluoxapiprolin 95 TC (the technical grade active ingredient) and Xivana Prime (the end-use product), containing the active ingredient fluoxapiprolin, for the control of late blight on potatoes, and against downy mildew and certain *Phytophthora* diseases on brassica head and stem vegetables, bulb vegetables, cucurbit vegetables, fruiting vegetables, leafy vegetables, leafy petiole vegetables, grapes and Amur river grapes.

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 fluoxapiprolin and Xivana Prime.

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

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

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

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

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

What is fluoxapiprolin?

Fluoxapiprolin is a new conventional fungicide active ingredient for disease management in a wide range of crops grown in Canada.

Health considerations

Can approved uses of fluoxapiprolin affect human health?

Xivana Prime, containing fluoxapiprolin, is unlikely to affect your health when used according to proposed label directions.

Potential exposure to fluoxapiprolin may occur through the diet (food and drinking water) or when handling and applying the end-use product or when coming into contact with treated surfaces. When assessing health risks, two key factors are considered: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are selected to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for 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 fluoxapiprolin was of low acute toxicity by the oral, dermal and inhalation routes. Fluoxapiprolin was non-irritating to the eyes and skin and did not cause an allergic skin reaction.

[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*.

The acute toxicity of the end-use product, Xivana Prime, containing fluoxapiprolin, was low via the oral, dermal and inhalation routes of exposure. It was non-irritating to the eyes and skin. It did cause 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 fluoxapiprolin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on the skeleton of developing rats. 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 estimate indicated that females 13–49 years are exposed to less than 1% of the acute reference dose (ARfD) for fluoxapiprolin, and therefore is 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 1% of the acceptable daily intake (ADI) for fluoxapiprolin, 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 22% of the acceptable daily intake for the metabolite fluoxapiprolin-BDM-pyrazole, 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 fluoxapiprolin is used according to the supported label directions, MRLs are being proposed as a result of this assessment (refer to PMRL2025-20, *Fluoxapiprolin*).

MRLs for fluoxapiprolin determined from the acceptable residue trials conducted throughout Canada and the United States, on potatoes, bulb onions, green onions, leaf lettuce, head lettuce, spinach, mustard greens, broccoli, cauliflower, cabbage, bell peppers, non-bell peppers, tomatoes, cucumbers, summer squash, muskmelons, grapes, celery, and strawberries can be found in the Science evaluation Section of this Document.

Occupational risks from Handling Xivana Prime

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

Workers mixing, loading or applying Xivana Prime, and workers entering recently treated fields can be exposed to fluoxapiprolin residues through direct skin contact and/or through inhalation. Therefore, the label specifies that anyone mixing and loading Xivana Prime and engaging in clean-up and repair activities must wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes. For applicators using handheld airblast/mist blowing equipment, chemical-resistant coveralls with a hood over a long-sleeved shirt, long pants, chemical-resistant gloves, socks and chemical-resistant footwear must also be worn. For all other application equipment, the applicator 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 entry into treated fields during the restricted-entry interval (REI) of 12 hours. Taking into consideration the label statements, the number of applications and the duration of exposure for handlers and postapplication workers, the risks to these individuals from exposure to Xivana Prime are not of health concern when the end-use product is used according to the proposed label directions.

Risks in residential and other non-occupational environments

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

Residential exposure to Xivana Prime is not expected, as it is not proposed for use in residential areas.

Health risks to bystanders

Bystander risks are not of health concern when Xivana Prime 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 fluoxapiprolin is introduced into the environment?

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

Fluoxapiprolin enters the environment when applied as a foliar spray to control or suppress certain oomycete diseases for various crops. Fluoxapiprolin is non-persistent to moderately persistent in aerobic soils and persistent in anaerobic soils. Fluoxapiprolin adsorbs strongly to soils and is not expected to move through the soil and reach groundwater. In water bodies,

fluoxapiprolin will move quickly to sediments where it is slightly persistent under aerobic conditions and moderately persistent under anaerobic conditions. Fluoxapiprolin is not expected to carry over to the next growing season. Fluoxapiprolin is a systemic fungicide; when applied as a spray, fluoxapiprolin can be absorbed and transported inside the plant. Fluoxapiprolin is not expected to be found in the air or to travel long distances from where it is applied. Fluoxapiprolin is not expected to build up in the tissues of organisms.

When used according to the label directions, fluoxapiprolin and its transformation products pose acceptable risk to non-target organisms, including small wild mammals, birds, beneficial insects including bees, earthworms, terrestrial and aquatic plants, amphibians, and freshwater and marine algae, fish, and invertebrates.

Value considerations

What is the value of Xivana Prime?

The registration of Xivana Prime will provide Canadian growers with a new mode of action fungicide to manage economically important and difficult-to-control diseases on the crops listed on the Xivana Prime label and is expected to contribute to resistance management.

Xivana Prime contains fluoxapiprolin as its sole active ingredient. It is effective against downy mildew and certain *Phytophthora* diseases when applied using ground application to brassica head and stem vegetables (Crop Group 5-13), bulb vegetables (Crop Group 3-07), cucurbit vegetables (Crop Group 9), fruiting vegetables (Crop Group 8-09), leafy vegetables (Crop Group 4-13), leafy petiole vegetables (Crop Subgroup 22B), and grape and Amur river grape. It is also effective against late blight on potato when applied using either ground or aerial application.

Measures to minimize risk

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

The key risk-reduction measures being proposed on the label of Fluoxapiprolin 95 TC and Xivana Prime 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 fluoxapiprolin through direct skin contact and inhalation of sprays, workers mixing, loading and applying Xivana Prime and performing cleaning and repair activities must wear the personal protective equipment (PPE) presented below.

The required personal protective equipment for Xivana Prime

Application equipment	Personal protective equipment	
	Mixer/Loader/Clean-up and repair	Applicator
Handheld airblast/mistblower[1]	Long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes.	Chemical-resistant coveralls with a chemical-resistant hood over long-sleeved shirt, long pants, chemical-resistant gloves, socks and chemical-resistant footwear.
All other application equipment[1]	Long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes.	Long-sleeved shirt, long pants, chemical-resistant gloves,[2] socks and shoes.

[1]For handheld equipment, wear eye, head and respiratory protection when applying above waist height, including overhead.
[2] Gloves are not required for application within a closed cab and/or cockpit.

The label also requires that workers do not enter or be allowed entry into treated fields during the REI of 12 hours. Risks to workers are not of health concern when Xivana Prime is used according to the proposed label directions and the restricted-entry interval is observed. Furthermore, a standard label statement to protect against drift during application is present on the label.

Environment

Standard best management practice statements will be included on the label to minimize risk.

Next steps

Before making a final registration decision on fluoxapiprolin and Xivana Prime, Health Canada's PMRA will consider any written comments received from the public that are directly related to this proposed decision, such as comments directed to the science evaluation, in response to this consultation document up to 30 days from the date of publication (Publications to add the publication date) of this document. If more time is required to provide comments, a request for an extension of up to 15 days can be made before the end of the original 30-day consultation period. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to PMRA Publications, through the Public Engagement Portal (Public Engagement 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

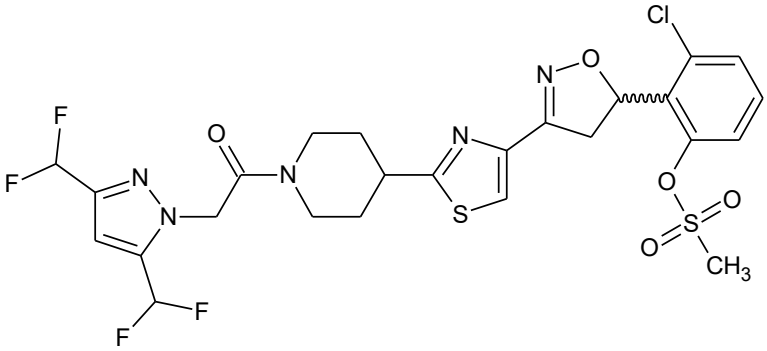
When Health Canada makes its registration decision, it will publish a Registration Decision on fluoxapiprolin and Xivana Prime (based on the Science evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection,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

Science evaluation

Fluoxapiprolin and Xivana Prime

1.0 The active ingredient, Its properties and uses

1.1 Identity of the active ingredient

Active substance	Fluoxapiprolin
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	2-{(*5RS*)-3-[2-(1-{[3,5-bis(difluoromethyl)-*1H*-pyrazol-1-yl]acetyl}-4-piperidyl)thiazol-4-yl]-4,5-dihydroisoxazol-5-yl}-3-chlorophenyl methanesulfonate
2. Chemical Abstracts Service (CAS)	2-[3,5-bis(difluoromethyl)-*1H*-pyrazol-1-yl]-1-[4-[4-[5-[2-chloro-6-[(methylsulfonyl)oxy]phenyl]-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]ethanone
CAS number	1360819-11-9
Molecular formula	$C_{25}H_{24}ClF_4N_5O_5S_2$
Molecular weight	650.07 g/mol
Structural formula	
Purity of the active ingredient	97.6 %

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

Technical Product—Fluoxapiprolin 95 TC

Property	Result
Colour and physical state	Light beige solid
Odour	Intense odour of solvents
Melting point	143.7°C
Boiling point or range	Decomposes prior to boiling
Density	1.51–1.56 g/cm^3
Vapour pressure at 20°C	3.0×10^{-5} Pa
Ultraviolet (UV)-visible spectrum	1) methanol λ max (nm) ε (L/(mol cm)) 204 5.26×10^4 2) methanol / 0.1 mol/L HCl (90/10, v/v) λ max (nm) ε (L/(mol cm)) 203 5.77×10^4 3) methanol/ 0.1 mol/L NaOH (90/10, v/v) λ max (nm) ε (L/(mol cm)) 220 2.74×10^4 No absorption observed above 300 nm
Solubility in water at 20°C	0.08 mg/L (in distilled water)
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) Heptane — 0.000061 Toluene — 1.1 Methanol — 1.3 Ethyl acetate — 15 Acetone — 84 Dichloromethane — 143 Dimethyl sulfoxide — >270
n-Octanol-water partition coefficient (K_{ow})	pH — log K_{ow} 4 — 3.4 7 — 3.4 9 — 3.4
Dissociation constant (pK_a)	Not applicable
Stability (temperature, metal)	Stable at 54°C in the presence of metals and metal ions

End-use product—Xivana Prime

Property	Result
Colour	Dark beige
Odour	Odourless
Physical state	Liquid

Property	Result
Formulation type	Suspension
Label concentration	20.0 g/L
Container material and description	HDPE bottle
Density	1.03–1.07 g/mL
pH of 1% dispersion in water	5.0–7.5
Oxidizing or reducing action	No an oxidizing or reducing substance
Storage stability	Stable on storage for 14 days at 54ºC and two years at ambient temperature in HDPE bottles
Corrosion characteristics	Not corrosive to HDPE bottles
Explodability	Not explosive

1.3 Directions for use

For the control or suppression of downy mildew and/or certain *Phytophthora* diseases on brassica head and stem vegetables (Crop Group 5-13), bulb vegetables (Crop Group 3-07), cucurbit vegetables (Crop Group 9), fruiting vegetables (Crop Group 8-09), leafy vegetables (Crop Group 4-13), and leafy petiole vegetables (Crop Subgroup 22B), Xivana Prime may be applied up to three applications per year on a 7- to 14-day re-application interval using ground application at 0.75 – 1.0 L product/ha, in accordance with all other label directions and restrictions.

For the control of downy mildew on grape and Amur river grape, Xivana Prime may be applied up to two times per year on a 10-day re-application interval using ground application at 0.75–1.0 L product/ha, in accordance with all other label directions and restrictions.

For the control of late blight on potato, Xivana Prime may be applied up to three times per year on a 7- to 14-day re-application interval using either ground or aerial application at 0.75–1.0 L product/ha, in accordance with all other label directions and restrictions.

For all labeled crops, a non-ionic surfactant at a rate of 0.125% v/v may be added to Xivana Prime for improved efficacy.

1.4 Mode of action

Fluoxapiprolin is classified in Group 49 by the Fungicide Resistance Action Committee (FRAC) as it acts as an oxysterol binding protein inhibitor (OSBPI) with medium to high risk of resistance development. It inhibits spore germination, germ tube elongation, penetration, mycelial growth, and sporangia formation.

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

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

Plant and animal matrices: HPLC-MS/MS methods (Method 01554, Method 01624 and Method TY-001-P18-01 in plant matrices, and Method 01628 in animal matrices) were developed and proposed for data gathering and enforcement purposes. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limits of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices. The proposed enforcement methods were successfully validated by independent laboratories. Adequate extraction efficiencies were demonstrated using bioincurred samples (primary crops: lettuce, grape, potato; rotational crops: wheat and turnip). For animal matrices, the solvents used in the proposed enforcement method are the same as those in the goat and hen metabolism studies, therefore, the enforcement method for animal matrices is expected to adequately extract bioincurred residues. Methods for residue analysis in plant and animal matrices are summarized in Appendix I, Table 1b.

3.0 Impact on human and animal health

3.1 Hazard assessment

3.1.1 Toxicology summary

Fluoxapiprolin is a piperidinyl-thiazole-isoxazoline fungicide that acts as a fatty acid amide hydrolase inhibitor via an oxysterol-binding protein in oomycetes.

A detailed review of the toxicology database for fluoxapiprolin was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. Additional studies were submitted to characterize potential effects on the endocrine system and to characterize the toxicity of certain metabolites. The required studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The human health risk assessment also considered any relevant scientific information found in the published literature. The scientific quality of the data is high and the database is considered adequate to characterize the potential health hazards associated with fluoxapiprolin. For metabolites of fluoxapiprolin, the scientific quality of the toxicology database is acceptable, and the database is considered adequate to characterize the majority of the toxic effects that may result from exposure.

Fluoxapiprolin is rapidly but poorly absorbed and exhibited evidence of saturation of toxicokinetic processes with increased dose and duration. There were significant sex differences in rats with higher C_{max} and area under the curve (AUC) values in males than in females. Tissue distribution was extensive and elimination was nearly complete. Of the radioactivity left in the carcass, the majority was found in the liver, skin, kidneys, lungs, plasma and blood cells. Excretion was rapid and primarily via the feces and bile with little urinary excretion. The majority of the administered dose was excreted as unchanged parent compound; however, the proposed metabolic pathway involves potential cleavage at any of the ring positions, as well as some defluorination and hydrolysis resulting in 22 minor metabolites including BCS-CS55621-4-OH and BCS-CS55621-acetamide, the metabolites monitored in the repeat-dose studies.

The applicant selected doses for many of the core studies based on a kinetically-derived maximum dose (KMD) approach. It was proposed that the absorption of fluoxapiprolin exhibits saturation starting at approximately 100 mg/kg bw/day resulting in concentrations of the parent compound and metabolites in the blood and tissues that are not proportionate to the increased dose. There are three types of dose response. A linear response to increased dose would result in the internal dose increasing at the same rate as the external dose and is considered the body's default pattern of absorption. On the other hand, a sublinear response would result in disproportionately lower internal concentrations than expected whereas a supralinear response would result in increasingly higher internal concentrations than expected in response to an increased external dose.

In rats, the levels of the parent compound and metabolites were disproportionately lower than the increase in dose in all matrices at or above the dose of 100 mg/kg bw/day. This effect was more pronounced in male rats after 14 days of treatment. When investigating the BCS-CC26002 metabolite, the pattern of absorption was sublinear as seen with the parent compound; however, the degree of sublinearity was higher after a single dose in male and female rats and also following repeated dosing in male rats than the parent compound resulting in even lower than expected concentrations. Following repeated dosing in females, the pattern of absorption of the BCS-CC26002 metabolite was closer to that of the parent compound. Uptake of the parent compound into all tissues was sublinear; however, concentrations in the liver, adrenals and ovaries were generally higher than plasma following repeated dosing while concentrations in the testes were much lower than in the plasma.

In the mouse, sublinearity of parent compound and metabolite concentrations were noted in the blood and plasma at a higher dose than in rats. Sex differences observed in the rats were not apparent in the mouse and there was no evidence of durational effects on absorption. In the tissues, sublinearity of absorption of the parent compound occurred at doses lower than plasma starting with the gonads and followed by the liver. In the mouse adrenals, sublinearity occurred at the same dose as plasma; however, there was evidence of linearity or supralinearity at the next lower dose.

Comparative microsomal liver assays indicated that in vitro metabolism by human liver microsomes did not differ from rat and dog liver microsomes to a notable extent. While the assays confirmed the sex differences in rats, liver microsomes from no other animal, including humans, exhibited differences in metabolism to the same extent as that observed with rat liver microsomes.

Acute toxicity of fluoxapiprolin was low via the oral, dermal and inhalation routes of exposure in rats. It was non-irritating to the eyes and skin of rabbits. It was not a dermal sensitizer in mice.

Xivana Prime was of low acute oral, dermal and inhalation toxicity in rats. It was non-irritating to the eyes and skin of rabbits. It was a dermal sensitizer in mice.

In short-term dietary toxicity studies, fluoxapiprolin was tested up to approximately the limit dose. Treatment-related findings in mice were limited to subacute mixed inflammation of the Harderian gland in both sexes with a slight increase in focal interstitial mononuclear cell infiltrate in males at dietary concentrations approaching the limit dose. In rats, short-term findings in dietary studies were limited to subacute chronic inflammation of the Harderian gland in males. At the highest dose tested, dogs exhibited decreased lactate dehydrogenase and increased glycogen in males and decreased red blood cells and haemoglobin in females. There were no treatment-related findings in the 28-day dermal toxicity study in rats up to the limit dose.

In the long-term and reproductive toxicity studies, the dose levels selected were lower than the traditionally-derived dose levels based on the maximum tolerated dose or the limit dose, and were based on a proposed saturation of absorption of fluoxapiprolin in the available studies. In the long-term rat and reproductive toxicity studies, the study investigators chose a high dose based on a value of approximately three- to five-fold higher than the proposed point of departure from dose-proportionality in rats. This point of departure was estimated based on results from a special 14-day bioanalytical study in rats performed to determine the saturation noted above and bioanalytical data from the guideline 90-day oral dietary toxicity study in the rat. In the long-term mouse toxicity study, the study authors chose a high dose based on the 14-day bioanalytical study in mice and the guideline 90-day oral dietary toxicity study in the mouse. The results of the 14-day bioanalytical study in the mouse indicated that the mouse exhibits saturation of absorption over the short-term at much higher doses than in the rat and doses up to the limit dose would have been appropriate in the long-term study. However, the authors asserted that the results of the 90-day study demonstrated saturation of toxicokinetic processes at lower dose levels following a longer duration of exposure. As such, the applicant attested that the same dose level in mice and rats would be sufficient to characterize the long-term toxicity and carcinogenic potential of fluoxapiprolin.

To support a dose selection rationale based on KMD considerations, toxicokinetic data must be sufficiently robust to clearly define the point at which toxicokinetic processes are overwhelmed. This may not necessarily be equivalent to the “inflection point” observed in non-linear toxicokinetics. The rationale was not accepted due to a number of issues including effects of the initial dose selection on the estimates of “expected internal dose” and concerns regarding the differences in toxicokinetic processes between male and female rats. It was determined that the acceptability of the dose level selection would be considered separately for each study taking into account toxicity in the entirety of the database and whether there would be value in additional studies testing higher doses.

In the long-term dietary mouse toxicity study, there were no treatment-related effects noted at the highest dose tested. While there were changes to the Harderian glands and liver at higher doses in 90-day study, there were no changes in the Harderian glands or liver or clinical chemistry changes that would indicate possible effects on the liver following 18 months of dietary exposure

and there was sufficient information to determine that fluoxapiprolin did not cause tumours in the mouse up to the highest dose tested. The highest dose tested was below the dose that would have been recommended based on the information provided; however, it was determined that the dosing was adequate for cancer assessment due to the lack of treatment-related findings in the 90-day study and lack of evidence of durational effects in the mouse. Additionally, while the toxicokinetic data did not confirm that the high dose would be above the point of inflection, at which point the increased external dose no longer results in a concomitant increase in internal dose levels, there was evidence of sublinear toxicokinetics.

In the long-term dietary rat toxicity study, there likewise were no effects noted up to the highest dose tested that were clearly related to treatment. There were low incidences of changes in the uterus including diffuse endometrial hyperplasia and a slight, non-statistically significant increase in uterine adenocarcinomas at the highest dose tested; however, they could not be definitively attributed to treatment and were considered equivocal. The dosing was adequate for cancer assessment as the non-cancer uterine effects were on the cusp of being considered treatment-related and there was evidence that higher doses would not result in substantially higher internal doses.

There was no evidence of genotoxicity of fluoxapiprolin in the standard battery of in vitro and in vivo assays.

As previously discussed, a slight increase in the incidence of uterine adenocarcinomas in females in the rat chronic dietary toxicity/oncogenicity study with fluoxapiprolin was considered equivocal based on the weight of evidence. Overall, the toxicology reference values selected for the non-cancer risk assessment are protective of any residual concerns regarding the carcinogenic potential of fluoxapiprolin.

In the dietary 2-generation reproductive toxicity study in rats, there were no effects in the parental, reproductive or offspring parameters up to the highest dose tested. Additional studies investigating endocrine-related endpoints were submitted on male and female immature rats as well as an in vitro steroidogenesis assay. There were no effects on uterine weights or vaginal opening at doses higher than those tested in the 2-generation reproductive toxicity study. In a supplementary Hershberger assay in males, organ weight effects in hormone-sensitive tissues were concurrent with and of the same magnitude as decreased body weights and occurred at doses higher than those tested in the 2-generation study. While decreased weights in hormone-sensitive tissues are generally considered to be of concern as these organ weights are unaffected by decreased body weights in adult animals, concern was lessened as the assay was performed in uncastrated and prepubertal animals, which do not conserve reproductive organ weights in the same manner. There were no effects on hormones in the steroidogenesis screen. The dosing was considered adequate for reproductive toxicity assessment based on the lack of findings at the highest dose tested, margins of 260-fold between the ADI, ARfD and highest doses tested and lack of effects on the endocrine system in special studies which used doses up to 1000 mg/kg bw/day (approaching the guideline limit doses).

In an oral gavage developmental toxicity study performed up to the limit dose in rats, there were no treatment-related findings in the maternal animals. There was an increase in the number of fetuses and litters that exhibited bent tails and short 14th thoracic ribs at the limit dose. Although these are well-characterized and not considered to be serious effects, they are occurring in the absence of maternal toxicity and indicate sensitivity of the young.

In an oral gavage developmental toxicity study performed in rabbits, there were no adverse effects noted in the maternal animals or fetuses up to the limit dose.

In an acute gavage neurotoxicity study in rats, there were no adverse effects noted at up to the limit dose. A waiver rationale was submitted for a subchronic neurotoxicity study. Based on the lack of acute neurotoxicity and lack of neurological effects in the rest of the database, the waiver was accepted. Likewise, a waiver for immunotoxicity studies was submitted and accepted based on the lack of effects on the immune system in the rest of the database.

Studies were conducted on a number of metabolites of fluoxapiprolin including BCS-BP32808 (3,5-bis(difluoromethyl)-1H-pyrazole; BCS-CS55621-BDM-pyrazole; fluoxapiprolin-BDM-pyrazole), BCS-CC26101 ([3,5-bis(difluoromethyl)-1H-pyrazol-l-yl]acetic acid; BCS-CS55621-pyrazole acetic acid), BCS-CZ38260 (5-(difluoromethyl)-1H-pyrazole-3-carboxylic acid; BCS-CS55621-pyrazole carboxylic acid), and BCS-CU97237 (4-[4-(5-{2-chloro-6-l(methylsulfonyl)oxy]phenyl}-4,5-dihydro-U-oxazol-3-yl)-1,3-thiazol-2-yl]piperidinium chloride; Cl- salt of BCS-CS55621-piperidine). BCS-CC26101, BCS-CZ38260 and BCS-CU97237 were assessed in in vitro genotoxicity assays and did not show evidence of genotoxicity. The weight of evidence was that BCS-BP32808 was not genotoxic due to the lack of genotoxicity in the in vivo micronucleus assay in the presence of significant clinical toxicity and marginal positive results in the AMES and in vitro micronucleus assays. However, it was of high acute oral toxicity and caused decreased body weight gain, clinical signs of toxicity and changes in clinical chemistry parameters at exceedingly low doses (5 mg/kg bw/day) compared to the parent compound in a 28-day oral toxicity study. As BCS-BP32808 was considered to be of higher toxicity than fluoxapiprolin, separate toxicology reference values were established for this metabolite for the dietary risk assessment.

The identification of select transformation products is presented in Appendix I, Table 2. The toxicology reference values for use in the human health risk assessment are summarized in Appendix I, Table 3. The toxicology reference value for the metabolite BCS-BP32808 is presented in Appendix I, Table 4. Results of the toxicology studies conducted on laboratory animals with fluoxapiprolin and relevant metabolites and with its associated end-use products, are summarized in Appendix I, Tables 5 and 6, respectively.

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.[5]

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the standard complement of studies was available, including gavage developmental toxicity studies in the rabbit and rat, and a dietary 2-generation reproductive toxicity study in the rat. The developmental toxicity studies in the rat and rabbit were performed up to the limit dose and the upper dose of the reproductive toxicity study was considered to be sufficient due to the margin of the ADI and ARfD to the high dose, lack of treatment-related effects in the study and lack of findings in the supplementary endocrine toxicity assays performed at higher doses than the 2-generation reproductive toxicity study.

With respect to potential prenatal and postnatal toxicity, there was some indication of increased sensitivity of fetuses compared to maternal animals in the rat developmental toxicity study. In the absence of maternal toxicity, there was an increase in bent tails and short 14th thoracic ribs, which were not considered serious effects. There were no treatment-related adverse effects identified in the 2-generation reproductive toxicity study in the rat or the rabbit developmental toxicity study.

Overall, the database is adequate for determining the sensitivity of the young. Although some effects occurred in the young fetus in the absence of maternal toxicity in the rat development toxicity study, they were well-characterized and were not serious in nature. Therefore, the *Pest Control Products Act* (PCPA) factor was reduced to threefold when using the rat developmental toxicity study to establish the point of departure for assessing risk to women of child-bearing age. For exposure scenarios for children, there were no treatment-related effects identified at the doses tested relevant to this age group and the points of departure selected for risk assessment were considered protective of potential effects in this subpopulation at higher doses. Therefore, the PCPA factor was reduced to onefold for this subpopulation.

3.2 Toxicology reference values

3.2.1 Route and duration of exposure

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

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

3.2.2 Occupational toxicology reference values

For the short- and intermediate-term dermal occupational risk assessment, the no observed adverse effect level (NOAEL) of 1000 mg/kg bw/day from the 28-day dermal toxicity study in rats was selected, which was the highest dose level tested in this study. This study was conducted via the relevant route and was of an appropriate duration of exposure. The dermal absorption was low, therefore, use of this study was considered protective of effects in the rat oral developmental toxicity study. For occupational and residential scenarios, the target margin of exposure (MOE) is 100, which includes standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of this study and target MOE is considered to be protective of all populations, including nursing infants and unborn children of exposed women.

For short- and intermediate-term occupational exposures via the inhalation route, the NOAEL of 300 mg/kg bw/day from the oral developmental toxicity study in the rat was selected for risk assessment. At 1000 mg/kg bw, there were increased incidences of bent tails and shortened 14th thoracic ribs in the fetuses in the absence of maternal toxicity. Worker populations could include pregnant or lactating women and therefore these endpoints were considered appropriate for the occupational risk assessment. A short-term inhalation toxicity study was not available, necessitating the use of an oral study for risk assessment.

In the absence of evidence to the contrary, absorption by the inhalation route is generally assumed to be 100%. In the case of fluoxapiprolin, toxicokinetic data suggest that uptake via the gastro-intestinal tract is very low at high dose levels (approximately 33%). Therefore, the oral NOAEL of 300 mg/kg bw/day, which represents an externally administered dose level, was adjusted to 99 mg/kg bw/day to correct for an approximate oral absorption of 33% to allow for extrapolation to systemic exposure estimates via the inhalation route.

The target MOE for these scenarios is 300, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability, as well as a factor of threefold for the reasons outlined in the *Pest Control Products Act* hazard characterization Section. 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 female workers.

3.2.3 Acute reference dose

Females 13–49 years of age

To estimate acute dietary risk of fluoxapiprolin to women of child-bearing age, the NOAEL of 300 mg/kg bw from the oral developmental toxicity study in the rat was selected for risk assessment. At 1000 mg/kg bw, there were increased incidences of bent tails and shortened 14th thoracic ribs in the fetuses in the absence of maternal toxicity. These effects were considered to potentially result from a single exposure and are therefore relevant to an acute risk assessment. 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:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{300 \text{ mg/kg bw}}{300} = 1 \text{ mg/kg bw of fluoxapiprolin}$$

General population (excluding females 13-49 years of age)

Establishment of an acute reference dose for fluoxapiprolin for the general population is not required, as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies that was relevant to the general population.

3.2.4 Acceptable daily intake (ADI)

To estimate risk following repeated dietary exposure to fluoxapiprolin, the NOAEL of 300 mg/kg bw/day from the oral developmental toxicity study in the rat was selected for risk assessment. At 1000 mg/kg bw/day, there were increased incidences of bent tails and shortened 14th thoracic ribs in the fetuses 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 ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{300 \text{ mg/kg bw/day}}{300} = 1 \text{ mg/kg bw/day of fluoxapiprolin}$$

The ADI provides margins of 260–374 to the highest dose levels tested in the 2-year rat and 18-month mouse chronic toxicity and carcinogenicity studies and in the 2-generation reproductive toxicity study.

3.2.5 Cancer assessment

As previously discussed, a slight increase in endometrial adenocarcinomas in females in the rat chronic dietary toxicity/oncogenicity study with fluoxapiprolin was considered equivocal based on the weight of evidence. Overall, the toxicology reference values selected for non-cancer risk assessment are protective of any residual concerns regarding carcinogenic potential of fluoxapiprolin.

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). For fluoxapiprolin, the aggregate assessment consisted of combining food and drinking water exposure only, since residential exposure is not expected. The most relevant toxicology endpoints and assessment factors for acute and chronic oral aggregate exposure are the same as those selected for the ARfD (see Section 3.2.3) and ADI (see Section 3.2.4), respectively.

Metabolite of toxicological concern - BCS-BP32808 (Fluoxapiprolin-BDM-pyrazole)

3.2.7 Acute reference dose for BCS-BP32808 metabolite

Establishment of an acute reference dose for the general population is not required, as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies with BCS-BP32808.

3.2.8 Acceptable daily intake (ADI) for BCS-BP32808 metabolite

To estimate risk following repeated dietary exposure to BCS-BP32808, the NOAEL of 2 mg/kg bw/day from the 28-day oral toxicity study in the rat was selected for risk assessment. At 5 mg/kg bw/day, there was decreased body weight gain in males and females and decreased body weight in females, increases in clinical signs of toxicity in males, decreased urea in males and decreased creatinine and increased potassium in females. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. Limited toxicology data were available for this metabolite, no long-term studies were provided. As a result, additional uncertainty factors of 10-fold for database deficiencies and threefold for extrapolation for study duration were applied. The CAF is thus 3000.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{2 \text{ mg/kg bw/day}}{3000} = 0.0007 \text{ mg/kg bw/day of BCS-BP32808}$$

3.3 Dermal absorption

Three studies were submitted as part of a triple pack for fluoxapiprolin, a rat in vivo study, and rat and human in vitro studies.

Overall, the studies were 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 PMRA position of accepting in vitro studies alone, when conducted using the standard methodology. The human in vitro study is considered acceptable for selecting a dermal absorption value for use in the exposure and risk assessment for fluoxapiprolin based on an analysis of the factors that can impact absorption (such as formulation, product composition, and doses).

A dermal absorption value of 3% from the lowest dose group (0.1 $\mu g/cm^2$) from the human in vitro study is recommended and supported by the results of the rat in vivo study. As this value is from the lowest dilution dose tested (0.1 $\mu g/cm^2$) and conducted with the proposed Canadian product, it addressed all proposed exposure scenarios for the fluoxapiprolin end-use product, Xivana Prime. Prior to applying this dermal absorption value to other end-use products, consideration of formulation type, product composition and doses is required. While a dermal absorption value was established, it was not used in the risk assessment since the dermal toxicological reference value for fluoxapiprolin is based on a dermal toxicity study.

3.4 Occupational and residential exposure assessment

3.4.1 Acute hazards of end-use product and mitigation measures

Xivana Prime

The acute hazard assessment indicated that Xivana Prime was of low acute oral, dermal and inhalation toxicity in rats. It was non-irritating to the eyes and skin of rabbits. It was a dermal sensitizer in mice. Based on these acute hazards, a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes must be worn by workers during mixing, loading, application, clean-up and repair activities.

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 fluoxapiprolin during mixing, loading, application, clean-up and repair. Dermal and inhalation exposure estimates were generated using the Agricultural Handlers Exposure Task Force (AHETF), the Pesticide Handlers Database (PHED, v1.1) and the Non-Dietary Task Force (NDETF) databases for mixers, loaders and applicators applying Xivana Prime using groundboom, airblast, aerial and various handheld equipment including airblast/mistblowers, backpack sprayers, manually-pressurized handwands and mechanically-pressurized handguns (Appendix I, Table 7). The PPE in the risk assessment is based on handlers wearing long pants, long-sleeved shirt, chemical-resistant gloves, socks and shoes, for all equipment types with the exception of handheld airblast/mistblowers, where handlers must also wear chemical-resistant coveralls with a hood.

Dermal and inhalation exposures were estimated by combining the unit exposure values with the amount of product handled per day. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight.

Exposure estimates were compared to the selected toxicology reference value to obtain the margin of exposure (MOE); the target MOE is 100 for the dermal route and 300 for the inhalation route. Dermal and inhalation MOEs were not combined since the dermal and inhalation reference values are not based on the same toxicological effects. Calculated dermal and inhalation MOEs are greater than the target MOEs of 100 and 300, respectively, for all chemical handler scenarios, and are therefore not of health concern (Appendix I, Table 8).

3.4.2.2 Postapplication exposure and risk assessment

There is potential for exposure to workers entering areas treated with Xivana Prime to complete tasks such as hand harvesting, hand weeding, hand set irrigation, girdling, etc. Given the nature of activities performed, exposure is primarily via the dermal route based on dermal contact with treated foliage. Inhalation exposure is not expected as fluoxapiprolin is considered non-volatile with a vapour pressure of 3×10^{-8} kPa at 20°C, 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).

As such, a quantitative inhalation risk assessment is not required. Inhalation risk is not of health concern for postapplication workers as fluoxapiprolin is considered to be non-volatile and the restricted-entry interval of 12 hours will allow residues to dry, suspended particles to settle and vapours to dissipate.

Chemical-specific data for assessing human exposures during postapplication activities specific to the various crops were not submitted. Therefore, the standard dislodgeable foliar residue (DFR) value of 25% of the application rate coupled with 10% daily dissipation of residues were used in the exposure assessment.

Dermal exposure to workers entering treated areas is estimated by combining DFR values with activity-specific transfer coefficients (TCs). The DFR values were based on the highest application rate 20 g a.i./ha, the greatest number of applications per season and shortest re-treatment interval for each crop/crop group. Activity-specific TCs are based on data from the Agricultural Re-entry Task Force (ARTF).

Exposure estimates were compared to the toxicology reference value to obtain the MOE; the target MOE is 100. Only exposures and risks to the activities with the highest TCs are presented as MOEs for these activities exceed the target MOE of 100, and are thus, not of health concern (Appendix I, Table 9). For all postapplication activities, the REI of 12 hours is adequate.

3.4.3 Residential exposure and risk assessment

3.4.3.1 Handler exposure and risk assessment

Xivana Prime 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

Xivana Prime is not a domestic class product and is not permitted for use in residential settings; therefore, a residential postapplication exposure assessment is not required.

3.4.4 Bystander exposure and risk assessment

Bystander exposure is considered negligible as application is limited when there is low risk of drift beyond the area to be treated, taking into consideration wind speed, wind direction, temperature inversions, application equipment, and sprayer settings. Therefore, bystander exposure and risk are not of health concern since the potential for drift is expected to be minimal.

3.5 Dietary exposure and risk assessment

3.5.1 Exposure from residues in food of plant and animal origin

The residue definition for enforcement in primary and secondary crops is fluoxapiprolin. The residue definition for risk assessment in primary crops is fluoxapiprolin and fluoxapiprolin-BDM-pyrazole (each assessed separately). The residue definition for risk assessment in secondary crops is fluoxapiprolin and fluoxapiprolin-pyrazole-alanine, expressed as parent equivalents. The residue definitions for enforcement and risk assessment for animal commodities

is fluoxapiprolin. The data gathering and enforcement analytical methods for plant and animal commodities are valid for the quantitation of fluoxapiprolin. The residues of fluoxapiprolin are stable in representative matrices from five commodity categories (high water (tomatoes), high oil (sunflower seeds), high protein (dry field pea seeds), high starch (potatoes) and high acid (grapes)) for up to 740 days/24 months when stored at ≤ -18°C. Therefore, fluoxapiprolin residues are stable in all raw agricultural commodities (RACs) and processed commodities for up to 740 days/24 months. Fluoxapiprolin residues concentrated in the following processed commodities only: dried tomatoes (5.3-fold), and raisins (3.3-fold). Quantifiable residues are not expected to occur in animal commodities based on the current use pattern. Crop field trials conducted throughout Canada and the United States using end-use products containing fluoxapiprolin at approved rates in or on potatoes, bulb onions, green onions, leaf lettuce, head lettuce, spinach, mustard greens, broccoli, cauliflower, cabbage, bell peppers, non-bell peppers, tomatoes, cucumbers, summer squash, muskmelons, grapes, and celery are sufficient to support the proposed maximum residue limits (MRLs). Field rotational crop studies were conducted in/on soybeans, turnips, wheat and strawberries. The data are adequate to demonstrate that a 30-day plantback interval (PBI) for strawberries, a 115-day PBI for small grain cereals, a 365-day PBI for non-labeled crops, and a restriction from rotating to root vegetables (Crop Subgroup 1A) are appropriate.

3.5.2 Exposure from residues in drinking water

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

Drinking water modelling follows a tiered approach consisting of progressive levels of refinement. Level 1 EECs are conservative values intended to identify 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 timing, and geographic scenario. Level 2 EECs are based on a narrower range of application timing, methods, and geographic scenarios, and are not considered conservative values that cover all regions of Canada.

Residues modelled and fate inputs

The drinking water residue definition was determined to include fluoxapiprolin and four major transformation products, BCS-CS55621-lactam, BCS-CS55621-pyrazole acetic acid, BCS-CS55621-4-OH-piperidine and BCS-CS55621-BDM-pyrazole (BCS-BP32808).

Drinking water modelling was conducted in two stages. First, fluoxapiprolin and three of its transformation products (BCS-CS55621-lactam, BCS-CS55621-pyrazole acetic acid, and BCS-CS55621-4-OH-piperidine) were modelled together as a combined residue due to assumed equal toxicity. Second, EECs of BCS-CS55621-BDM-pyrazole were modelled separately. Although BCS-CS55621-BDM-pyrazole was observed in one of six soils used in the laboratory studies, its

toxicity is higher than the parent. Therefore, a conservative approach was taken by assuming that BCS-CS55621-BDM-pyrazole was sprayed directly on the crops at an application rate of 16 g/ha, equivalent to the maximum annual application rate of the parent compound of 60 g a.i./ha when adjusted for molecular weight. The major fate inputs used for the drinking water modelling are outlined in Appendix I, Tables 10 and 11.

Estimated environmental concentrations in drinking water

Modelling was performed at Level 1. The use pattern selected for the modelling was a single application of 60 g a.i./ha/year. A single use pattern intended to represent all proposed uses was considered. EECs for surface water were calculated based on a single standard scenario. EECs in 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.

Level 1 EECs for fluoxapiprolin and metabolite fluoxapiprolin-BDM-pyrazole, expressed as parent equivalent, are reported in Appendix I, Tables 12 and 13, respectively.

3.5.3 Dietary risk assessment

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

3.5.3.1 Acute dietary exposure results and characterization

The basic acute analysis was conducted using proposed Canadian MRLs and/or US Tolerances as well as default processing factors. For the secondary crop, strawberry, the highest average field trial (HAFT) residue from the field accumulation study was used for the combined residues of fluoxapiprolin and fluoxapiprolin-pyrazole-alanine.

The basic acute dietary exposure for all supported fluoxapiprolin commodities was estimated to be 0.56% of the ARfD for Females 13-49 years (95th percentile, deterministic). Aggregate exposure from food and drinking water (EEC value = 16 µg a.i./L, Level 1, ground water [peak]) is not of health concern. Specifically 0.61% of the ARfD was obtained for Females 13-49 years.

3.5.3.2 Chronic dietary exposure results and characterization

Fluoxapiprolin

The following assumptions were applied to the basic chronic analysis for fluoxapiprolin: 100% crop treated, MRL values for all crops except the secondary crop, strawberry, where the supervised trial median residue (STMdR) residue from the field accumulation study for the combined residues of fluoxapiprolin and fluoxapiprolin-pyrazole-alanine were used, and default processing factors (where available). The basic chronic dietary exposure (food alone) from all supported fluoxapiprolin food commodities for the total population, including infants and children, and all representative population subgroups is 0.3% of the acceptable daily intake (ADI). Aggregate exposure from food and drinking water is considered acceptable. The PMRA

estimates that chronic dietary exposure to fluoxapiprolin from food and drinking water is 0.2% (0.002 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1-2 years at 0.3% (0.003 mg/kg bw/day) of the ADI.

Fluoxapiprolin-BDM-pyrazole

The following assumptions were applied to the refined (intermediate level) chronic analysis for fluoxapiprolin-BDM-pyrazole: 100% crop treated, default processing factors (where available) and residues in/on all crops based on supervised trial median residue (STMdR) values. The refined (intermediate level) chronic dietary exposure (food alone) from all supported 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). Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to fluoxapiprolin-BDM-pyrazole from food and drinking water is 9% (0.00006 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1–2 years at 22% (0.00015 mg/kg bw/day) of the ADI.

3.6 Aggregate exposure and risk assessment

For fluoxapiprolin, the aggregate assessment consisted of combining food and drinking water exposure only, since residential exposure is not expected.

3.7 Cumulative assessment

The *Pest Control Products Act* requires the PMRA to consider the cumulative effects of pest control products that have a common mechanism of toxicity. Accordingly, an assessment of a potential common mechanism of toxicity with other pest control products was undertaken for fluoxapiprolin. Fluoxapiprolin is a piperidinyl-thiazole-isoxazoline fungicide, and the only other pesticide registered in Canada or the US in that class is oxathiapiprolin. Findings in the oxathiapiprolin database were limited to generalized toxicity, such as effects on body weight, and there are currently no molecular or mechanism of action data to establish a common mammalian mechanism of toxicity between fluoxapiprolin and other pest control products.

The PMRA did not identify information indicating that fluoxapiprolin shares a common mechanism of mammalian toxicity with other pest control products and it does not appear to produce a toxic metabolite in common with other pest control products. Therefore, a cumulative assessment is not required at this time.

3.8 Maximum residue limits

Dietary risks from the consumption of food commodities listed in Table 3.8.1 were shown to be acceptable when fluoxapiprolin is used according to the supported label directions. Therefore, foods containing residues at these levels are safe to eat, and the PMRA recommends that the following MRLs be specified for residues of fluoxapiprolin.

Table 3.8.1 Recommended maximum residue limits

MRL (ppm)	Food commodity
6.0	Leafy vegetables (Crop group 4-13, except head lettuce)
2.0	Green onions (Crop subgroup 3-07B)
1.5	Leaf petioles vegetables (Crop subgroup 22B)
0.8	*Brassica* head and stem vegetables (Crop group 5-13), head lettuce
0.5	Raisins
0.2	Small fruits vine climbing except fuzzy kiwifruit (Crop subgroup 13-07F), dried tomatoes
0.07	Cucurbit vegetables (Crop group 9)
0.06	Fruiting vegetables (Crop group 8-09)
0.03	Bulb vegetables (Crop subgroup 3-07A)
0.01	Eggs, fat, meat and meat byproducts of cattle, goats, hogs, horses, poultry and sheep, milk, tuberous and corm vegetables (Crop subgroup 1C), strawberries

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 animal and plant matrices, analytical methodologies, field trial data, and acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1b, 14 and 15.

3.9 Health incident reports

As of March 2025, no human or domestic animal incidents involving the active ingredient fluoxapiprolin were submitted to the PMRA.

4.0 Impact on the environment

4.1 Fate and behaviour in the environment

Fluoxapiprolin has low water solubility (0.08 mg/L at 20°C), low vapor pressure (3.0×10^{-5} Pa at 20ºC), and a low Henry's law constant of 2.4×10^{-6} atm m^3 mol^{-1}. Volatilization is not expected to be a significant route of dissipation. Fluoxapiprolin does not undergo abiotic transformation at an appreciable rate under Canadian-relevant environmental conditions (Appendix I, Table 16).

In terrestrial environments, fluoxapiprolin is non-persistent to moderately persistent in aerobic soils, forming carbon dioxide, four major transformation products and three minor transformation products, as well as non-extractable residues (NERs) (Appendix I, Table 16). Of the four major transformation products, BCS-CS55621-piperidine and BCS-CS55621-lactam are persistent, BCS-CS55621-BDM-pyrazole is non-persistent to slightly persistent, while BCS-

CS55621-pyrazole acetic acid is non-persistent in aerobic soils. Of the three minor transformation products, BCS-CS55621-thiazole acid is moderately persistent to persistent, BCS-CS55621-pyrazole carboxylic acid is non-persistent, and no kinetic data are available for BCS-CS55621-4-OH-piperidine but its maximum concentrations were detected before the end of the studies. Fluoxapiprolin is persistent in anaerobic soils. Fluoxapiprolin and its transformation products have low leaching potential, either due to strong adsorption to soil matrices or short half-lives. The laboratory study results are supported by the results from field studies where fluoxapiprolin was slightly persistent to moderately persistent and minimum residues were detected in soil depths below 15 cm. Therefore, fluoxapiprolin is not expected to carry over to the following growing season and has low likelihood to move through soil and reach groundwater.

In aquatic environments, fluoxapiprolin partitions rapidly from the water column to the sediment layer, where it is slightly persistent under aerobic conditions and moderately persistent under anaerobic conditions. Four major aquatic transformation products, BCS-CS55621-lactam, BCS-CS55621-pyrazole acetic acid, BCS-CS55621-pyrazole carboxylic acid, and BCS-CS55621-4-OH-piperidine, were observed under aerobic conditions; all of which were also observed in the aerobic soil studies. In addition, two unique major transformation products, BCS-CS55621-keto-hydroxy and BCS-CS55621-dihydroxy, were formed under anaerobic conditions and predominantly resided in the sediment.

Fluoxapiprolin is not expected to be found in the air or to travel long distances from where it is applied based on its low vapour pressure and Henry's law constant. This was supported by negligible amount of volatilization observed in the laboratory studies.

Fluoxapiprolin is not expected to build up in the tissues of organisms based on low BCF values determined in a bioconcentration study in fish.

The fate and behaviour of fluoxapiprolin and its transformation products in the environment are summarized in Appendix I, Table 16.

4.2 Environmental risk characterization

An environmental risk assessment was conducted as described in the PMRA 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 the effects metrics.

EECs were estimated using standard models that consider application rate(s) and environmental fate properties of the pesticide, including pesticide dissipation between applications. For the end use product, Xivana Prime, the proposed maximum use pattern, representing the most conservative exposure scenario, was considered in this risk assessment (3 applications of 20 g a.i./ha (the highest single application rate) at 7-day intervals per growing season). Fluoxapiprolin dissipation between applications was accounted for using a soil half-life of 59.8 days (90% upper confidence bound on the mean of 13 representative soil half-lives), a water/sediment half-life of 48.6 days (the 80th percentile of 4 representative half-lives), or a default foliar dissipation half-life of 10 days, respectively, resulting in cumulative yearly application rates (total application

rate accumulated over a year accounting for dissipation between applications) of 55.4, 54.5 and 39.9 g a.i./ha for soil, water/sediment and plants, respectively. The estimated EECs in various media are summarized in Appendix I, Table 17, and are used in the risk assessment. EECs for transformation products were calculated assuming 100% conversion from the parent compound with adjustment for molar ratios without dissipation between applications (Appendix I, Table 17).

The effects metrics were calculated by adjusting toxicity endpoints with uncertainty factors (UF). 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). All available acute and chronic ecotoxicological data for non-target terrestrial, freshwater and marine organisms are summarized in Appendix I, Table 18 and 19, respectively. The toxicity endpoints and UFs used to establish the effects metrics, along with the level of concern (LOC) used in the risk assessment are presented in Appendix I, Table 20.

A screening-level risk assessment was performed to identify specific uses that do not pose a risk to non-target organisms. The screening-level risk assessment used 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 LOC. As all screening level RQs were below the LOC, the risk was considered to be acceptable, and no further risk characterization was necessary.

4.2.1 Risks to terrestrial organisms

Terrestrial organisms, such as earthworms, pollinators, beneficial arthropods, birds, small wild mammals, and terrestrial non-target vascular plants can be exposed to fluoxapiprolin through direct contact with spray, spray drift, run-off, contact with sprayed surfaces, or from ingestion of contaminated food. Screening level exposure for terrestrial invertebrates considers direct spray application on soil or plant surfaces at the maximum cumulative yearly application rates accounting for dissipation between applications (Appendix I, Table 17).

A risk assessment of fluoxapiprolin and the associated end-use product, Xivana Prime, was undertaken based on toxicity data obtained from available studies. In addition, risk assessments for major transformation products observed in laboratory fate studies were also performed. A summary of the effects on terrestrial organisms considered in the selection of toxicity endpoints is provided in Appendix I, Table 18. For the screening level risk assessment, the most sensitive endpoints for each taxon selected as surrogates are presented in Appendix I, Table 20, together with the effects metrics and respective uncertainty factors and level of concern. Toxicity studies on earthworms, collembola and honey bees showed that most of the transformation products had endpoints less sensitive than fluoxapiprolin, and therefore, their assessments were covered by the parent compound. For the few exceptions where the transformation products had more sensitive endpoints than the parent compound, assessments were conducted for the respective taxa. A summary of screening level risk quotients and level of concern for fluoxapiprolin and its transformation products is presented in Appendix I, Tables 21–23.

Earthworms: Fluoxapiprolin was not toxic to earthworms on an acute or chronic basis at a concentration of 945 mg a.i./kg soil dw when tested with the technical grade compound. However, reduced body weight was observed when tested with a formulated product at 1000 mg

end-use product/kg soil dw (19.2 mg a.i./kg soil dw). The risk quotient for earthworms resulting from acute and chronic exposure to fluoxapiprolin in soil did not exceed the level of concern at the screening level (Appendix I, Table 21). Of the seven transformation products tested, only BCS-CS55621-BDM-pyrazole showed significant reduction of numbers of juveniles, resulting in a NOEC of 32 mg/kg soil dw. As this endpoint is less sensitive compared to fluoxapiprolin content in end-use products, no further risk assessment was conducted for the transformation products. The risk to earthworms from use of fluoxapiprolin has been determined to be acceptable.

Beneficial arthropods: Laboratory studies showed that when arthropods were exposed to residues on glass plates, fluoxapiprolin, applied at concentrations equivalent to 60 g a.i./ha, was non-toxic to the standard arthropod species *Aphidius rhopalosiphi* but showed some toxicity to *Typhlodromus pyri* (15.7% mortality at 60 g a.i./ha). Additional tests for soil dwelling species exposed to fluoxapiprolin residues in soil did not result in any toxicity effects. The risk quotients for predatory and parasitic arthropods resulting from exposure to fluoxapiprolin either on plant or on soil surfaces did not exceed the level of concern at the screening level.

Of the seven transformation products tested, BCS-CS55621-BDM-pyrazole and BCS-CS55621-thiazole acid exhibited toxicity to the killer mite (*Hypoaspis aculeifer*) and collembolan (*Folsomia candida*). Of the two, BCS-CS55621-BDM-pyrazole was more toxic and resulted in increased mortality and reduced reproduction. The most sensitive endpoint, an EC_{10} of 8.1 mg/kg soil dw for the collembolan, was used in risk assessment. The risk quotients for beneficial arthropods resulting from exposure to BCS-CS55621-BDM-pyrazole did not exceed the level of concern at the screening level.

Risk quotients for these organisms are presented in Appendix I, Table 21. The risk to beneficial arthropods from use of fluoxapiprolin has been determined to be acceptable.

Pollinators: Fluoxapiprolin may be found in pollen and nectar as spray droplets are deposited onto open flowers during foliar application or through translocation inside plants. For honey bees representing pollinators, the exposure at the screening level is based on a single maximum application rate of 20 g a.i./ha and the estimated exposures on a per bee basis using default values and consumption rates for adult and larval honey bees (Appendix I, Table 17). The single application rate is used to calculate EECs. This is because individual flowers generally only bloom for a short period of time and they are therefore unlikely to be sprayed with fluoxapiprolin more than once.

Fluoxapiprolin was practically non-toxic to honey bees on an acute contact and oral basis. No mortality or sublethal effects were observed in adult or larval bees from chronic exposure to technical grade fluoxapiprolin; however, mortality and reduced adult emergence were observed in adult and larval bees, respectively, from chronic exposure to a formulated product, resulting in a 10-day no observed adverse effects dose (NOAED) of 12 µg a.i./bee/day for adult bees, and a 22-day NOAED of 4.8 µg a.i./bee/day for larval bees. The four fluoxapiprolin transformation products tested were all practically non-toxic to honey bees on an acute contact and acute oral basis. BCS-CS55621-pyrazole-methylsulfinyl acid, a plant metabolite, was the only transformation product that had an apparently more sensitive endpoint for acute contact toxicity compared to the parent compound, as the toxicity test was conducted at a lower concentration range. However, no toxic effects were observed, and the LD_{50} was greater than the highest test

concentration (Appendix I, Table 18). Since BCS-CS55621-pyrazole-methylsulfinyl acid is a plant metabolite, the potential for contact exposure was considered very low. Furthermore, accounting for molecular weight differences (224.2 g/mole compared to 650.1 g/mole for fluoxapiprolin), its contact exposure EEC would be approximately one third of the parent compound EEC on a mass basis, assuming 100% transformation and availability for contact exposure. Therefore, the risk of BCS-CS55621-pyrazole-methylsulfinyl acid to bees is expected to be no more than that of the parent compound.

In addition to honey bees, acute oral and contact toxicity of fluoxapiprolin to bumble bees was tested. No effects were observed when tested with the active ingredient; but food avoidance was observed when tested with formulated product. The endpoints obtained from bumble bees were less sensitive than those from honey bees. Therefore, the risk assessment for honey bees is adequately representative of bumble bees.

The screening level (Tier I) risk quotients for adult honey bees from acute contact, acute oral, and chronic exposure and for larval bees from acute oral and chronic exposure did not exceed the level of concern (Appendix I, Table 22). The Tier I risk assessment is supported by results from the semi-field studies (Tier II), which showed no significant or biologically relevant effects on any measurement endpoint evaluated from foliar application of fluoxapiprolin (Appendix I, Table 18). The risks associated with the use of fluoxapiprolin have been determined to be acceptable for pollinators.

Birds: Fluoxapiprolin was non-toxic to birds up to the highest test dose on an acute basis either through acute oral administration or by sub-acute dietary consumption (Appendix I, Table 18). The formulated product was also non-toxic to birds on an acute basis through acute oral administration; however, it provided the most sensitive endpoint based on content of the active ingredient and was used for risk assessment. Fluoxapiprolin did not have chronic effects nor effects on reproduction. The screening level risk was assessed considering direct application at the maximum cumulative yearly rate accounting for dissipation between applications of 39.9 g a.i./ha on plant surfaces (Appendix I, Table 17). Concentrations of fluoxapiprolin on various food items used to determine the amount of pesticide in the diet or the estimated daily exposure (EDE) are presented in Appendix I, Table 17. The risk quotients for birds with generic body weights (small (20 g), medium (100), and large (1000 g)) resulting from acute oral, dietary and reproductive exposure to fluoxapiprolin did not exceed the level of concern at the screening level (Appendix I, Table 23). The risk to birds from use of fluoxapiprolin has been determined to be acceptable.

Mammals: Fluoxapiprolin was practically non-toxic to rats on an acute basis, with an oral LD_{50} of > 5000 mg a.i./kg bw. Tests with the formulated product also showed no toxic effects up to the highest test dose through acute oral administration (5000 mg end-use product/kg bw, equivalent to 96 mg a.i./kg bw). Because the formulated product provided the most sensitive endpoint based on content of the active ingredient, it was used for the risk assessment (Appendix I, Table 18). A two-generation rat reproduction study resulted in a female parental and offspring NOAEL of 262 mg a.i./kg bw/day as the most sensitive endpoint. Observed treatment-related effects included irregular estrous cycles and delay in vaginal opening for the parent rats and offspring, respectively.

The screening level risk was assessed considering direct application at the maximum cumulative yearly rate accounting for dissipation between application of 39.9 g a.i./ha on plant surfaces. Concentrations of fluoxapiprolin on various food items used to determine the amount of pesticide in the diet or the EDE are presented in Appendix I, Table 17. The risk quotients for mammals with generic body weights (small (15 g), medium (35 g), and large (1000 g)) resulting from acute oral and reproductive exposure to fluoxapiprolin did not exceed the level of concern at the screening level (Appendix I, Table 23).

Tests with the soil transformation product, BCS-CS55621-BDM-pyrazole, showed that it was moderately toxic to rats on an acute basis (Appendix I, Table 18), with an oral LD_{50} value of 175 mg/kg bw. Clinical signs from acute oral exposure included decreased activity, hunched posture, piloerection, incoordination and cold to touch. In a 28-day repeated dietary study, BCS-CS55621-BDM-pyrazole resulted in a NOAEL of 2 mg/kg bw/day. Observed treatment-related effects included decreased body weight gain, decreased food intake and reduced motor activity (Appendix I, Table 18). It is noted that BCS-CS55621-BDM-pyrazole was only observed in one of six aerobic soils, and as such, the potential for exposure to mammals through contaminated food is expected to be limited.

The screening level risk was assessed considering the annually applied amount of fluoxapiprolin would be completely transformed to BCS-CS55621-BDM-pyrazole instantaneously. The risk quotients for mammals resulting from acute and chronic exposure to BCS-CS55621-BDM-pyrazole did not exceed the level of concern at the screening level (Appendix I, Table 23).

The risk to mammals from use of fluoxapiprolin has been determined to be acceptable.

Terrestrial vascular plants: In the seedling emergence and vegetative vigour studies with a fluoxapiprolin formulated product, little or no effect on the germination, emergence, survival and growth of ten plant species was observed at the tested rate of 150 g a.i./ha. Considering the maximum cumulative yearly in-field EECs from a direct spray on soil surfaces (55.4 g a.i./ha) or on plants (39.9 g a.i./ha), accounting for dissipation between applications (Appendix I, Table 17), the risk quotients did not exceed the level of concern for in-field exposure (Appendix I, Table 21). The risk to terrestrial vascular plants from use of fluoxapiprolin has been determined to be acceptable.

4.2.2 Risks to aquatic organisms

Aquatic organisms, such as invertebrates, fish, plants and algae can be exposed to fluoxapiprolin through spray drift or runoff. A risk assessment of fluoxapiprolin and the associated end-use product was undertaken based on available toxicity data for freshwater and marine invertebrates, fish, plants and algae. Acute toxicity data for eight transformation products were available for daphnia and freshwater algae and were included in the risk assessment.

A summary of the effects on aquatic organisms considered in the selection of toxicity endpoints is provided in Appendix I, Table 19. The most sensitive endpoints for each taxon selected as surrogates for the screening level risk assessment are presented in Appendix I, Table 20, together with the effects metrics and respective uncertainty factors and the levels of concern. The screening level risk assessment for fluoxapiprolin is presented in Appendix I, Table 24.

It should be noted the acute toxicity endpoint values were largely attributed to the experimentally achieved solubility of fluoxapiprolin technical, depending on if solvent was used and the type of solvent used (limit of functional solubility). All acute endpoints for fluoxapiprolin were non-definitive, with "greater than" values, and little or no effects were observed up to the highest tested concentrations. When tested with a formulated product, higher test concentrations could be achieved. Even with the formulated product, it was not feasible to achieve exposure concentrations high enough to cause acute toxicity for many species. Results from studies conducted with formulated product suggest that the true endpoints would be higher than those obtained from studies using the active ingredient. Similarly, for those transformation products with low solubilities, the acute toxicity endpoints were non-definitive endpoints where no effects were observed at the highest test concentrations achieved in the studies.

Invertebrates: Fluoxapiprolin was non-toxic to aquatic invertebrates up to the experimental limit of solubility on an acute basis. Chronic effects were observed for pelagic invertebrates with a NOAEC of 0.032 mg a.i./L for *Daphnia magna* and for benthic invertebrates with a NOAEC of 0.02 mg a.i./L for *Hyalella azteca* (overlying water) and 0.0437 mg a.i./L for *Chironomus riparius* (pore water). The risk quotients for acute and chronic exposure of pelagic invertebrates to fluoxapiprolin did not exceed the level of concern at the screening level. The risk quotients for acute and chronic exposure of benthic invertebrates to fluoxapiprolin in overlying water and pore water did not exceed the level of concern at the screening level.

For the eight transformation products tested for acute toxicity to daphnia, BCS-CS55621-lactam, which had the same solubility as the parent compound, had the most sensitive EC_{50} of > 0.658 mg/L (the highest test concentration) and was used to represent all transformation products in the risk assessment. The risk quotient for acute exposure of pelagic arthropods to BCS-CS55621-lactam did not exceed the level of concern at the screening level.

Definitive endpoints were determined for two soluble transformation products, BCS-CS55621-piperidine and BCS-CS55621-BDM-pyrazole, with EC_{50} values of 14.7 and 42 mg/L, respectively. Based on these endpoints, the two transformation products were classified as moderately and slightly toxic to daphnia, respectively. However, these endpoints were orders of magnitude higher than fluoxapiprolin and BCS-CS55621-lactam, and therefore, a separate risk assessment was not conducted.

The risk to aquatic invertebrates from use of fluoxapiprolin has been determined to be acceptable.

Fish: Fluoxapiprolin had no acute or chronic effects on freshwater fish at concentrations up to the highest test concentration at the experimental limit of solubility (Appendix I, Table 19). The risk quotients for freshwater fish resulting from acute exposure and chronic exposure at early-life stages to fluoxapiprolin did not exceed the level of concern at the screening level.

For saltwater fish, acute exposure to fluoxapiprolin at the experimental limit of solubility had no toxic effect. Chronic exposure of early-life stages of fish to fluoxapiprolin did not result in statistically-significant effects on reproduction and survival, but there were statistically-significant reductions in fish total length and dry weight, with the most sensitive NOEC at 0.23 mg a.i./L (Appendix I, Table 19).

The risk quotients for saltwater fish resulting from acute exposure and chronic exposure at early-life stages to fluoxapiprolin did not exceed the level of concern at the screening level (Appendix I, Table 24).

The risk to freshwater and saltwater fish from use of fluoxapiprolin has been determined to be acceptable.

Amphibians: Using endpoints obtained from acute and early-life stage studies with fish as surrogate, along with an EEC for fluoxapiprolin in a 15-cm deep body of water, the risk quotients for amphibians did not exceed the level of concern at the screening level. Results from a qualitative amphibian metamorphosis assay (Tier-I test for endocrine disruptor) for the African clawed frog (*Xenopus laevis*) provided support for this assessment as no apparent treatment-related histopathologic effects in the thyroid glands were observed up to 0.83 mg a.i./L on Day 7 and Day 43 (Nieuwkoop-Faber (NF) stage 62). This concentration is more than 20 times higher than the screening level EEC. The risk to amphibians from use of fluoxapiprolin has been determined to be acceptable.

Algae: Fluoxapiprolin and its formulated product had inhibition effects on some species of freshwater and marine algae, with the most sensitive IC_{50} of > 0.91 mg a.i./L and IC_{05} of 0.398 mg a.i./L for *Pseudokirchneriella subcapitata*. The risk quotients for freshwater algae resulting from acute and chronic exposure to fluoxapiprolin and for marine algae resulting from acute exposure to fluoxapiprolin did not exceed the level of concern at the screening level.

For the eight transformation products tested for acute toxicity to freshwater algae, seven had higher endpoint values than fluoxapiprolin. The exception was BCS-CS55621-lactam, which had a more sensitive EC_{50} of > 0.537 mg/L for *Pseudokirchneriella subcapitata* due to the solubility limit, though the effect was growth promotion rather than inhibition at all test concentrations. As such, the risk of exposure to the transformation products to algae was covered by the assessment for the parent compound. The risk to algae from use of fluoxapiprolin has been determined to be acceptable.

Aquatic vascular plants: No dose-responsive effects on aquatic vascular plants were observed for either technical grade fluoxapiprolin or a formulated product up to its experimentally achieved solubility under the test conditions. Using the most sensitive endpoint (IC_{50} > 0.952 mg a.i./L for *Lemna gibba*), the risk quotients for aquatic vascular plants resulting from acute exposure to fluoxapiprolin did not exceed the level of concern at the screening level. The risk to aquatic vascular plants from use of fluoxapiprolin has been determined to be acceptable.

4.2.3 Environmental incident reports

As of March 2025, no environmental incident reports involving fluoxapiprolin have been submitted to the PMRA.

5.0 Value

Fluoxapiprolin is a new conventional active ingredient for disease management in Canada. Currently, other fungicides are registered for managing oomycete diseases on vegetable crops on the Xivana Prime label. Xivana Prime will provide Canadian vegetable growers with a new mode of action to manage economically important and difficult-to-control oomycete diseases on labelled crops and is expected to contribute to resistance management.

Scientific rationales and results from field trials testing the efficacy of Xivana Prime, when applied alone or tank mixed with a non-ionic surfactant, on broccoli, brussels sprouts, cabbage, onion, cucumber, melon, gourd, tomato, bell pepper, jalapeno pepper, lettuce, potato, and grape demonstrated the value for label claims against downy mildew and *Phytophthora* diseases on brassica head and stem vegetables (Crop Group 5-13), bulb vegetables (Crop Group 3-07), cucurbit vegetables (Crop Group 9), fruiting vegetables (Crop Group 8-09), leafy vegetables (Crop Group 4-13), leafy petiole vegetables (Crop Subgroup 22B), potato, grape and Amur river grape.

No phytotoxicity or injury to the crops was observed in the trial studies. When used according to label directions, application of Xivana Prime is not expected to result in any non-safety adverse effects to the labelled crops.

Details of the supported uses can be found in Appendix I, Table 25.

6.0 Pest Control Product Policy considerations

6.1 Toxic Substances Management Policy considerations

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

During the review process, fluoxapiprolin and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[6] and evaluated against the Track 1 criteria. Health Canada has reached the conclusion that fluoxapiprolin and its transformation products do not meet all the TSMP Track 1 criteria. Refer to Appendix I, Table 26 for further information on the TSMP assessment.

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

6.2 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the 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.*[7] The list is used as described in the PMRA Science Policy Note SPN2020-01[8] and is based on existing policies and regulations, including the *Toxic Substance Management Policy* and *Formulants Policy*,[9] and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives Regulations* under the *Canadian Environmental Protection Act* (substances designated under the *Montreal Protocol*).

Health Canada has reached the conclusion that Fluoxapiprolin 95 TC does not contain any contaminants identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. The end-use product, Xivana Prime, contains the preservative 1,2-benzisothiazolin-3-one which contains low levels of dioxins and furans. These are being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of the TSMP.

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

7.0 Proposed regulatory decision

Health Canada's PMRA, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Fluoxapiprolin 95 TC and Xivana Prime, containing the technical grade active ingredient fluoxapiprolin, for the control of late blight on potatoes, and against downy mildew and certain *Phytophthora* diseases on brassica head and stem vegetables, bulb vegetables, cucurbit vegetables, fruiting vegetables, leafy vegetables, leafy petiole vegetables, grapes and Amur river grapes.

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.

Additional information being requested

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

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7 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.*

8 PMRA's 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

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

List of abbreviations

↑	increased
↓	decreased
♂	male
♀	female
^{14}C	Carbon-14 radioactive isotope
°C	degrees Celsius
µm	micrometre(s)
µg	microgram(s)
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
ADME	absorption, distribution, metabolism and elimination
AHETF	Agricultural Handlers Exposure Task Force
ANG	water-sediment system identifier (Germany)
AOPWIN	Atmospheric Oxidation Program for Microsoft Windows
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
atm	atmosphere
ATPD	area treated per day
AUC	area under the curve
AX	soil identifier (German)
BAF	bioaccumulation factor
BBCH	Biologishe Bundesanstalt, Bundessortenamt and Chemical industry
BCF	bioconcentration factor
BCF_K	kinetic bioconcentration factor
BCF_{SS}	steady-state bioconcentration factor
BCS-CS55621	fluoxapiprolin
bw	body weight
bwg	body weight gain
C_{max}	highest blood concentration
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
CG	crop group
CI	confidence interval
cm	centimetre(s)
cm^3	cubic centimetre(s)
CMC	carboxymethylcellulose
CO_2	carbon dioxide
CSG	crop subgroup
CR	chemical-resistant
d	day(s)
DD	soil identifier (German)
DDA	days after daytime application

DEEM	Dietary Exposure Evaluation Model
DFOP	double first-order in parallel
DFR	dislodgeable foliar residue
DOC	dissolved organic carbon
DT_{50}	dissipation time 50% (time required to observe 50% decline in concentration)
dw	dry weight
EC_{10}	effective concentration on 10% of the population
EDC	endocrine disrupting chemical
EDE	estimated daily exposure
EEC	estimated environmental concentration
ELS	early life-stage
ER_{25}	effective rate on 25% of the population
ER_{50}	effective rate on 50% of the population
F_0	parental generation
F_1	first generation
F_2	second generation
fc	food consumption
FCID	Food Commodity Intake Database
FIR	food ingestion rate
FRAC	Fungicide Resistance Action Committee
g	gram(s)
GD	gestation day
GL	water-sediment system identifier (USA)
GR	water-sediment system (USA)
ha	hectare(s)
HAFT	highest average field trial
Hb	hemoglobin
HC	historical control data
HDPE	high density polyethylene
HDT	highest dose tested
HH	soil identifier (German)
HN	soil identifier (German)
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
hr(s)	hour(s)
IC_{05}	inhibitive concentration on 5% of the population
IC_{50}	inhibitive concentration on 50% of the population
ILV	independent laboratory validation
IORE	Indeterminate Order Rate Equation
IUPAC	International Union of Pure and Applied Chemistry
K_d	soil-water partition coefficient
kg	kilogram(s)
KMD	kinetically-derived maximum dose
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
kPa	kilopascal
L	litre(s)

LAFT	lowest average field trial
LC_{50}	concentration estimated to be lethal to 50% of the test population
LD_{50}	dose estimated to be lethal to 50% of the test population
LDH	lactate dehydrogenase
LLNA	local lymph node assay
LNE	soil identifier (US)
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOEC	lowest observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
M/L/A	mixer/loader/applicator
m^2	square metre(s)
m^3	cubic metre(s)
MAS	maximum average score for 24, 48 and 72 hours
MBq	megabecquerel
mg	milligram(s)
MIS	maximum irritation score
mL	millilitre(s)
MOE	margin of exposure
MRL	maximum residue limit
MWHC	maximum water holding capacity
N/A	not applicable
NAFTA	North American Free Trade Agreement
NDETF	Non-dietary Exposure Task Force
NER	non-extractable residues
Ng	nanogram
NHANES	National Health and Nutrition Examination Survey
nm	nanometre(s)
NOAEC	no observed adverse effect concentration
NOAED	no observed adverse effects dose
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOER	no observed effect rate
OC	organic carbon content
OECD	Organisation for Economic Co-operation and Development
OSBPI	Oxysterol binding protein inhibitor
Pa	Pascal
PBI	plantback interval
PCA	soil identifier (US)
PCPA	*Pest Control Product Act*
peq	parent equivalent
pH	measure of the acidity or basicity of an aqueous solution
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval

PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
RAC	raw agricultural commodity
RBC	red blood cells
REI	restricted-entry interval
RQ	risk quotient
S9	mammalian metabolic activation system
SDEV	standard deviation
SFO	single first-order
STMdR	supervised trial median residue
tbw	terminal body weight
TC	transfer coefficient
TP	transformation product
t_R	representative half-life
TRR	total radioactive residue
TSMP	*Toxic Substances Management Policy*
TWA	time-weighted average
US	United States
USEPA	United States Environmental Protection Agency
v/v	volume per volume dilution
VOC	volatile organic compounds
W	watt(s)
w/w	weight per weight
WIE	water-sediment system identifier (Germany)
wt	weight
WWEIA	What We Eat in America

Appendix I Tables and figures

Table 1a Residue analysis in environmental media

Matrix	Method ID	Analyte	Method type	LOQ	Reference
Soil/Sediment	TY-003-S20-01	BCS-CS55621 (active)	HPLC-MS/MS	0.5 ng/g	PMRA No. 3349324
		BCS-CY96288		0.5 ng/g	
		BCS-DC21250		0.5 ng/g	
		BCS-DA63612		0.5 ng/g	
		BCS-CC26101		0.5 ng/g	
		BCSCZ38260		0.5 ng/g	
		BCS-BP32808		0.5 ng/g	
		BCS-DG91934		0.5 ng/g	
Water	TY-004-W21-01	BCS-CS55621 (active)	HPLC-MS/MS	0.5 ng/mL	PMRA No. 3401652
		BCS-CY96288		0.5 ng/mL	
		BCS-DC21250		0.5 ng/mL	
		BCS-DA63612		0.5 ng/mL	
		BCS-CC26101		0.5 ng/mL	
		BCSCZ38260		0.5 ng/mL	
		BCS-BP32808		0.5 ng/mL	
		BCS-DG91934		0.5 ng/mL	

Table 1b Residue analysis in plant and animal matrices

Analytical methods	Matrices	Analyte	Method ID/Type	LOQ	Reference (PMRA No.)
Livestock commodities					
Enforcement method	Poultry (egg, skin with fat), bovine (muscle, liver, kidney, whole milk, cream)	Fluoxapiprolin	Method 01628/ HPLC-MS/MS	0.01 ppm	3349586
ILV of enforcement method	Poultry (egg, skin with fat), bovine (liver, milk)				349589

Analytical methods	Matrices	Analyte	Method ID/Type	LOQ	Reference (PMRA No.)
Plant commodities					
Data-gathering methods	Tomatoes, grapes, potatoes, sunflower seeds, dry field pea seed, barley straw	Fluoxapiprolin	Method 01554/HPLC-MS/MS	0.01 ppm	3349582
			Method TY-001-P18-01/HPLC-MS/MS (based on Method 01554)	0.01 ppm	3349583
	Grapes, tomato, potato tuber, field peas, sunflower seed	Fluoxapiprolin enantiomers: BCS-CX87605 (enantiomer S) BCS-CX87606 (enantiomer R)	Method 01634/HPLC-MS/MS	0.01 ppm	3473319
Enforcement method	Tomatoes, grapes, potatoes, sunflower seeds, dry field pea seed, barley straw	Fluoxapiprolin	Method 01624 /HPLC-MS/MS	0.01 ppm	3349587
ILV of enforcement method	Tomatoes, sunflower seeds	Fluoxapiprolin	Method 01624/ HPLC-MS/MS	0.01 ppm	3349588
Radiovalidation	Primary crops: head lettuce , grapes, potatoes, Secondary crops: wheat (forage, straw, grain), turnips (roots, greens)	Fluoxapiprolin	Method 01624 and Method 01554/ HPLC-MS/MS	0.01 ppm	3349592

Table 2 Identification of select transformation products of fluoxapiprolin

Code	Chemical name	Source
BCS-BP32808 (BCS-CS55621-BDM-pyrazole; fluoxapiprolin-BDM-pyrazole)	3 ,5-bis(difluoromethyl)-1H-pyrazole	Aerobic soil transformation product, animal metabolite (hen fat), plant metabolite (green onions)

Code	Chemical name	Source
BCS-CC26101	[3,5-bis(difluoromethyl)-1H-pyrazol-l-yl]acetic acid	Aerobic soil and aerobic water/sediment transformation product, minor rat metabolite
BCS-CZ38260	5-(difluoromethyl)-1H-pyrazole-3-carboxylic acid	Aerobic water/sediment transformation product, aerobic soil transformation product, minor rat metabolite
BCS-CU97237	4-[4-(5-{2-chloro-6-l(methylsulfonyl)oxy]phenyl}-4,5-dihydro-U-oxazol-3-yl)-1,3-thiazol-2-yl]piperidinium	Aerobic soil transformation product

Table 3 Toxicology reference values for use in health risk assessment for fluoxapiprolin

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or Target MOE
Acute dietary females 13–49	Rat developmental toxicity study	Developmental NOAEL = 300 mg/kg bw/day ↑ bent tails in the absence of maternal toxicity and ↑ short 14th thoracic rib	300
ARfD (females 13–49) = 1 mg/kg bw/day			
Acute dietary general population	Establishment of an acute reference dose is not required, as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies.		
Repeated dietary	Rat developmental toxicity study	Developmental NOAEL = 300 mg/kg bw/day ↑ bent tails in the absence of maternal toxicity and ↑ short 14th thoracic rib	300
ADI (general population) = 1 mg/kg bw/day			
Short- and intermediate-term dermal	Rat 28-day dermal toxicity study	NOAEL = 1000 mg/kg bw/day No adverse effects up to the highest dose tested	100

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or Target MOE
Short- and intermediate-term inhalation[2]	Rat developmental toxicity study	Adjusted NOAEL = 99 mg/kg bw/day, based on a developmental NOAEL of 300 mg/kg bw/day corrected for 33% oral absorption ↑ bent tails in the absence of maternal toxicity and ↑ short 14th thoracic rib	300
Cancer	Equivocal increase in endometrial adenocarcinomas in rats. Toxicology reference values selected for non-cancer risk assessment are protective of any residual concerns regarding carcinogenic potential.		

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

2 Since GI absorption was only approximately 33% at 10 mg/kg bw/day and compound absorption by the inhalation route is assumed to be 100%, the original oral NOAEL of 300 mg/kg bw/day was multiplied by a 33% correction factor to obtain a systemic NOAEL (300 × 0.33 = 99) for inhalation exposure scenario.

Table 4 Toxicology reference values for use in health risk assessment for BCS-BP32808 metabolite

Exposure scenario	Study	Point of departure and endpoint	CAF[1] or Target MOE
Acute dietary general population	Establishment of an acute reference dose is not required, as an endpoint of concern attributable to a single exposure was not identified in the oral toxicity studies.		
Repeated dietary	Rat 28-day dietary toxicity study	NOAEL = 2 mg/kg bw/day Decreased body weight, increased clinical signs and changes in clinical chemistry findings	3000
ADI (general population) = 0.0007 mg/kg bw/day			

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

Table 5 Toxicity profile of technical fluoxapiprolin

Effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to body weights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.

Study type/Animal/PMRA No.	Study results
Toxicokinetic studies	
Pilot metabolism on [Acetyl-2-^{14}C] BCS-CS55621 PMRA No. 3349245 [Pyrazole-4-^{14}C]BCS-CS55621 – Absorption, distribution, metabolism and excretion in the rat. PMRA No. 3349246 [Phenyl-UL-^{14}C]BCS-CS55621 – Absorption, distribution, excretion and metabolism in the rat PMRA No. 3349243 [Pyrazole-4-14C]BCS-CS55621 – tissue retention PMRA No. 3349244 [pyrazole-4-14C]BCS-CS55621 – Tissue distribution and excretion of radioactivity in the rat by quantitative whole body autoradiography PMRA No. 3349247	ADME studies were performed on acetyl-, pyrazole- and phenyl-labelled BCS-CS55621 as preliminary or main studies at single gavage doses of 0.62, 5, 10 or 200 mg/kg bw. A repeat dose assay was performed with 14 days of 10 mg/kg bw/d gavage doses of unlabelled BCS-CS55621 followed by a single gavage 10 mg/kg bw dose of pyrazole-labelled BCS-CS55621 and a tissue retention study was performed at 200 mg/kg bw/day in ♂ and ♀ for 10 days and 200, 500 or 1000 mg/kg bw/day in ♂ for three days. Absorption was rapid but low and exhibited saturation with increased dose level and duration of dosing. There were significant sex differences with higher Cmax and AUC values in ♀ than in ♂. Tissue distribution was extensive and elimination was nearly complete. Of the radioactivity remaining at 72 hours post-dosing, the majority was found in the liver, carcass, skin, kidneys, lungs, plasma and blood cells. In an autoradiography study, concentrations in the tissues peaked at 4 hours in ♂and 1 hour in ♀, were below the limit of detection in most tissues by 48 hours, and by 168 hours radioactivity was only persistent in the bile ducts, bone surface, liver, renal cortex, trachea and urinary bladder wall. Excretion was rapid and primarily in the feces followed closely by the bile, and urinary excretion was very low. The majority of the administered dose (AD) was excreted as unchanged BCS-CS55621; however, when metabolized, it was extensive with 22 identified peaks. In the pyrazole- and phenyl-labelled studies, the second most common compound following unchanged BCS-CS55621 was BCS-CS55621-4-OH; however, the metabolite measured in the toxicity studies was only observed in the acetyl-labelled studies, BCS-CS55621-acetamide (BCS-CC26002). There were no new metabolites found in the tissues following repeated dosing. Absorption following pretreatment in the repeat dose assay was lower than following single low doses. In a tissue retention study, there was no evidence of tissue retention at 200, 500 or 1000 mg/kg bw/day. At 1000 mg/kg bw/day, excretion was slower than at 200 or 500 mg/kg bw/day. The proposed metabolic pathway involves the hydroxylation of the piperidine ring at position 4 to form BCS-CS55621-4-OH piperidine and subsequent cleavage of the bond between piperidine and thiazole rings, oxidation to BCS-CS55621-piperidine-carboxylic acid, defluorination and oxidation to 3-carboxylic acid and opening of the piperidine ring to form BCS-CD55621-pyrazole-acetamide or

Study type/Animal/PMRA No.	Study results
	BCS-CS55621-pyrazole-acetamide-COOH. The phenyl ring is hydroxylized at positions 2, 3, and 4, defluorination followed by oxidation to a 3-carboxylic acid, piperidine ring opening and oxidation forming a 3-OH-propyl side chain, oxidation of the 3-OH-propyl side chain leading to a pentanoic acid, thiazole ring opening forming a isoxazole-glycolic acid, further decarboxylation of the isoxazole-glycolic acid to a isoxazole group, and cleavage between the oxazole moiety and the phenyl ring by oxidation to a benzoic acid and conjugation with glucuronic acid in position 1. Other positions are subject to glucuronidation or conjugation with cysteine. The hydrolysis of the piperidyl moiety results in a 3-OH-propyl side chain which is further oxidized into a pentanoic acid-group and either of the di-fluoromethyl groups may be oxidized into carboxylic acid.
14-day bioanalytical study (dietary) PMRA No. 3349248	Rats were given BCS-CS55621 at doses of 0, 400, 1000, 2600, 6500 or 13000 ppm in the diet (33.7/35.3, 87/85.2, 223/235, 557/574 and 1050/1164 mg/kg bw/day for ♂/♀) for 14 days to monitor plasma concentrations of unchanged BCS-CS55621 and the major metabolite, BCS-CC26002, after a single or repeated dosing. The liver, adrenals and gonads were analyzed for unchanged BCS-CS55621 and metabolite concentrations at the end of the dosing period. The linear relationship between the plasma concentration of each analyte and the administered dose was investigated. Sublinearity of unchanged BCS-CS55621 and metabolite concentrations were noted in all matrices tested starting at the second dose of approximately 90–100 mg/kg bw. Sublinearity of unchanged BCS-CS55621 was consistent between ♂and ♀ after a single dose but was exaggerated in ♂ following 14 days of treatment. Plasma concentrations of the metabolite exhibited a larger difference from the expected after a single dose in ♂ and ♀ and repeated dosing in ♂; however, the sublinearity observed in repeated-dose ♀ was more similar to unchanged BCS-CS55621. Uptake of unchanged BCS-CS55621 into the liver, adrenals and ovaries was sublinear but concentrations of BCS-CS55621 were orders of magnitude higher in these tissues than in the plasma. Uptake into the testes exhibited a more exaggerated sub-linearity than plasma and the other tissues, as such BCS-CS55621 concentrations were comparatively very low in the testes.
14-day bioanalytical study (dietary) PMRA No. 3349178	Mice were given BCS-CS55621 at doses of 0, 220, 560, 1400, 3500 or 7000 ppm in the diet (equal to 0/0, 32.7/35.0, 82.3/87.4, 208/236, 506/602 and 1044/1143 mg/kg bw/day) for 14 days to monitor plasma concentrations of the unchanged BCS-CS55621 and the major metabolite, BCS-CC26002, after a single or repeated dosing. The liver, adrenals and gonads were analyzed for unchanged BCS-

Study type/Animal/PMRA No.	Study results
	CS55621 and metabolite concentrations at the end of the dosing period. The linear relationship between the plasma concentration of each analyte and the administered dose was investigated. Unchanged BCS-CS55621 concentrations in plasma were supra-linear in male and female mice up to and including 1400 ppm (208/236 mg/kg bw/day) and sub-linear in ♂ at 3500 ppm (506 mg/kg bw/day) and in ♀ at 7000 ppm (999 mg/kg bw/day) after 2 days and 3500 ppm (598 mg/kg bw/day) after 14 days. Supra-linearity was exaggerated in ♂, but was relatively unaffected by repeat dosing. BCS-CC26002 concentrations plateaued at 3500 ppm (506/602 mg/kg bw/day). Tissue concentrations of the unchanged BCS-CS55621 were linear to supra-linear at 560 ppm in the liver and 1400 ppm in the adrenals and sublinear thereafter. Concentrations were sublinear in the testes at 1400 ppm and in the ovaries at 560 ppm, ovaries having the most exaggerated sublinearity and the lowest concentrations.
Interspecies comparison studies (in vitro) PMRA No. 3349249 PMRA No. 3349250 PMRA No. 3349251	Liver microsomes from ♂and ♀rats, dogs and humans were incubated with 0.5 µmol/L or 0.1 µmol/L labelled-fluoxapiprolin for 0, 60 or 120 minutes. The recovery of radioactivity was determined as relative percentages of the applied radioactivity recovered in the supernatant of the specific incubates as compared with the initial radioactivity. The incubates were analyzed via HPLC to quantify the metabolites as peaks; however, the peaks were not further identified as to chemical structure. A positive control group using 10 µmol/L [4-^{14}C]testosterone adequately validated the system. [thiazolyl-2-^{14}C]Fluoxapiprolin Three minor metabolites were found in male human liver and 4 minor metabolites were found in female human liver. No single unique metabolite was present at over 2.5%. Human ♂ metabolized similar amounts of unchanged BCS-CS55621 as rats and dogs, human ♀ had much lower residual unchanged BCS-CS55621 compound, and ♀ rats had the most residual unchanged BCS-CS55621 compound. [pyrazole-4-^{14}C]Fluoxapiprolin Human microsomes exhibited fewer sex differences than in rats and dogs. No human unique metabolites [phenyl-UL-^{14}C]Fluoxapiprolin Least amount of biotransformation in female rat liver, fewer sex differences in humans and dogs than rats. No unique human metabolites.

Study type/Animal/PMRA No.	Study results
Acute toxicity studies	
Acute oral toxicity (Up and Down procedure) Crl:WI Wistar rats PMRA No. 3349163	LD_{50} > 5000 mg/kg bw (♂♀) Low acute oral toxicity There were no clinical signs of toxicity.
Acute dermal toxicity Crl:WI Wistar rats PMRA No. 3349165 DER	LD_{50} > 2000 mg/kg bw (♂♀) Low acute dermal toxicity There were no clinical signs of toxicity.
Acute inhalation toxicity Crl:WI Wistar rats PMRA No. 3349166	LC_{50} > 2.11 mg/L (♂♀) Low acute inhalation toxicity One male and one female died following exposure to 5.10 mg/L test substance. Clinical signs of toxicity in surviving animals consisted of laboured respiration, wet fur, red-brown staining around the nose and/or cranium, noisy respiration, ruffled fur, decreased activity and/or dyspnea. All signs of toxicity abated by Day 3.
Eye irritation study New Zealand White rabbits PMRA No. 3349167	$MIS_{(1hr)}$ = 4/110 $MAS_{(24\text{-}72hrs)}$ = 0/110 Non-irritating to the eye
Dermal irritation study New Zealand White rabbits PMRA No. 3349168	$MIS_{(1hr)}$ = 0/8 $MAS_{(24\text{-}72hrs)}$ = 0/8 Non-irritating to the skin
Dermal sensitization - LLNA CBA/CaOlaHsd mice PMRA No. 3349169	Negative
Short-term toxicity studies	
28-day range-finding dietary toxicity study C57BL/6J mice	Acceptable with limitations No treatment-related effects observed up to 1024/1132 mg/kg bw/day (♂/♀)

Study type/Animal/PMRA No.	Study results
PMRA No. 3349175	Limitations: only 5 animals/sex/group; not subject to Quality Assurance statements
90-day dietary toxicity study C57BL/6J mice PMRA No. 3349170	NOAEL = 171/222 mg/kg bw/day (♂/♀) LOAEL = 882/1079 mg/kg bw/day (♂/♀) Effects at the LOAEL included ↑ unilateral subacute mixed inflammation of Harderian gland (♂♀); ↑ focal interstitial mononuclear cell infiltrate in the liver (♂) Toxicokinetics: Plasma was analyzed for BCS-CS55621, BCS-CC26101 and BCS-CC26002 at Week 12 and presented as mean plasma concentrations. Animals had quantifiable concentrations of the test substance and BCS-CC26002 metabolite in the plasma at all doses and plasma concentrations increased in a dose-responsive but sublinear manner. The BCS-CC26101 metabolite was found at the limit of quantification only at the top dose. There were no sex differences.
28-day range-finding dietary toxicity study Wistar rats PMRA No. 3349174	Acceptable with limitations No treatment related effects observed up to 942/1111 mg/kg bw/day (♂/♀). Limitations: only 5 animals/sex/group; not subject to Quality Assurance statements
90-day dietary toxicity study Wistar rats PMRA No. 3349171	NOAEL = 175 mg/kg bw/day (♂) / 1169 mg/kg bw/day (♀) LOAEL = 891mg/kg bw/day (♂) / undetermined (♀) Effects at the LOAEL: ↑ in subacute to chronic inflammation of Harderian glands (♂) Toxicokinetics: Plasma was analyzed for test substance, BCS-CC26002 and BCS-CC26101 at week 14 and presented as mean plasma concentrations. Absorption of the test substance was relatively low. Other than the test substance in ♀ and the BCS-CC26002 metabolite in high-dose ♂, levels were below the limit of quantification in one to four animals per dose group regardless of the analyte. Where a mean concentration could be calculated, there was a dose-responsive, but sub-linear, increase in plasma concentrations in the test substance and the metabolites.
28-day range-finding dietary toxicity study Beagle dogs	Acceptable with limitations No treatment-related effects observed up to 1011/994 mg/kg bw/day (♂/♀)

Study type/Animal/PMRA No.	Study results
PMRA No. 3349176	Toxicokinetics: Plasma was analyzed on Day 28 for BCS-CC55621, BCS-CC26101 and BCS-CC26002 and presented as individual plasma concentrations. Demonstrated internal exposure to all analytes with evidence of saturation of absorption. Peak in BCS-CS55621 concentrations between 6–24 hours, peak in both metabolite concentrations between 1-2 hours post-administration. Limitations: only 2 animals/sex/dose; not subject to Quality Assurance statements
90-day dietary toxicity study Beagle dog PMRA No. 3349173	NOAEL = 272/270 mg/kg bw/day (♂/♀) LOAEL = 892/895 mg/kg bw/day (♂/♀) Effects at the LOAEL: ↓ LDH, ↑ glycogen (♂); ↓ RBC, Hb (♀) Toxicokinetics: Plasma was analyzed for BCS-CS55621, BCS-CC26101 and BCS-CC26002 at Week 13 and presented as mean Tmax, Cmax, AUC and clearance values. The analytes were found in the plasma of all treated animals. Absorption of BCS-CS55621 was sublinear in ♂ and ♀; however, absorption continued to increase with dose at the top dose and the clearance was higher in ♀ than ♂. BCS-CS26101 was found at lower levels than BCS-CC55621; however, exposure was higher in ♀ than ♂ with a higher clearance. Absorption was linear. Overall exposure to BCS-CC26002 was lower in ♀ than in ♂, although the clearance was higher in ♀. Absorption of BCS-CC26002 was linear in males and supralinear in females.
28-day dermal toxicity study Wistar rats PMRA No. 3349179	NOAEL = 1000 mg/kg bw/day HDT LOAEL – undetermined
28-day inhalation toxicity study Waiver rationale PMRA No. 3349180	Accepted based on the lack of acute inhalation toxicity, low toxicity by the oral route and large margins of exposure when using the oral study for the inhalation risk assessment.
Chronic Toxicity/oncogenicity studies	
18-month chronic and carcinogenicity dietary study C57BL/6J mice	NOAEL = 278/317 mg/kg bw/day HDT (♂/♀) LOAEL = not established No adverse effects up to HDT

Study type/Animal/PMRA No.	Study results
PMRA No. 3349181	**No evidence of carcinogenicity** Toxicokinetics: Plasma was analyzed for BCS-CS55621 and BCS-CC26002 at Days 91, 355 and 540 and reported as mean plasma concentrations. BCS-CS55621 was found in plasma of all treated animals and increased in a dose-responsive, but sublinear, manner in ♂♀. Plasma concentrations of BCS-CS55621 increased with duration in all ♀ dose groups, but not in ♂ and the BCS-CS55621 concentrations were highest in ♀. BCS-CC26002 – found in plasma of all treated animals, dose responsive but sublinear ♂♀, no change in concentration with duration, plasma concentrations equivalent or slightly higher than BCS-CS55621 in ♂, plasma concentration slightly lower with duration in ♀.
24-month dietary chronic and carcinogenicity study Wistar rats PMRA No. 3349182	NOAEL = 288/374 mg/kg bw/day HDT (♂/♀) LOAEL = undetermined Note: ♂ sacrificed two weeks early due to high mortality in all groups. Endometrial adenocarcinoma in uterus 0/60, 0/60, 1/60 (1.7%), 3/60 (5%) - equivocal Equivocal evidence of carcinogenicity Toxicokinetics: Plasma was analyzed at Days 88, 353 and 701 for BCS-CS55621 and BCS-CC26002 and reported as AUC. BCS-CS55621 was found in the plasma of all treated animals. It was at higher concentrations in ♀ than ♂ by an order of magnitude. Concentrations were dose responsive with exception of 88 day high-dose ♂, however, the increase was sublinear at later time points BCS-CC26002 was detected in plasma of all treated animals and at lower concentrations in ♀ than ♂, but concentrations in males and females were within same order of magnitude. The concentrations were dose responsive but sublinear at all time points.
Developmental/reproductive toxicity studies	
Range-finding dietary reproductive toxicity study	Acceptable with limitations

Study type/Animal/PMRA No.	Study results
Han Wistar rat PMRA No. 3349185	Parental: 260/279 mg/kg bw/day (♂/♀): ↓ combined uterus, cervix and oviduct wts F_0 (♀); ↑ kidney pelvic dilatation F_1 (♀) Reproductive: No treatment-related effects observed in reproductive parameters up to 260/279 mg/kg bw/day (♂/♀) Offspring: 279 mg/kg bw/day: ↑ kidney pelvic dilatation F_1 (♀) Toxicokinetics (F_0 animals only): Plasma was analyzed for BCS-CS55621 and BCS-CC26002 at the end of Week 4 (premating), Gestation Day 17 and Lactation Day 18 and presented as mean plasma concentrations. BCS-CS55621 was found in plasma of all treated F_0 animals at higher concentration in ♀ than ♂ by an order of magnitude. Concentrations were sublinear but increased with dose and there were lower plasma concentrations during lactation BCS-CC26002 was found in plasma of all treated F_0 animals and at slightly higher plasma concentrations in ♂. Concentrations increased in a dose-responsive but sublinear manner and there was no change in ♀ over premating, gestation and lactation. Limitations: 8 animals/sex/dose; single generation mated; limited post-mortem examination of F_0 generation; limited investigation of F_1 generation including termination after sexual maturation
2-generation dietary reproductive toxicity study Han Wistar rat PMRA No. 3349184	Parental: NOAEL = 262/302 mg/kg bw/day HDT (♂/♀) LOAEL - undetermined Reproductive: NOAEL = 262/302 mg/kg bw/day HDT (♂/♀) LOAEL - undetermined Offspring: NOAEL = 302 mg/kg bw/day HDT LOAEL – undetermined No evidence of sensitivity of the young Toxicokinetics: Plasma was analyzed for BCS-CS55621 and BCS-

Study type/Animal/PMRA No.	Study results
	CC26002 in parental F_0 and F_1 animals at Week 10 (premating), Gestation Day 17, Lactation Day 18 and at PND 21 of the unselected F_1 and F_2 offspring and presented as mean plasma concentrations and normalized plasma concentrations. BCS-CS55621 – found in plasma of all treated animals, higher concentration in ♀ than ♂ by an order of magnitude, sublinear increases with dose, no change in plasma concentrations in ♀ over premating, gestation and lactation BCS-CC26002 – found in all treated animals, double the plasma concentrations in ♂ than ♀, sublinear increases with dose, no change in ♀ over premating, gestation and lactation.
Range-finding gavage developmental toxicity study Sprague Dawley rats PMRA No. 3349187	Acceptable with limitations Maternal toxicity: There were no treatment-related effects up to 1000 mg/kg bw/day Offspring/developmental toxicity: There were no treatment-related effects up to 1000 mg/kg bw/day Limitations: 8 dams/dose; only external and skeletal examinations of the fetuses were performed and only in the control and high-dose groups
Developmental gavage toxicity study Sprague Dawley rats PMRA No. 3349186	**Maternal NOAEL =** 1000 mg/kg bw/day (HDT) **Maternal LOAEL** - undetermined **Fetal/developmental NOAEL:** 300 mg/kg bw/day **Fetal/developmental LOAEL:** 1000 mg/kg bw/day 1000 mg/kg bw/day: ↑ bent tails, ↑ short 14th thoracic rib Evidence of sensitivity of the young No treatment-related malformations
Range-finding gavage developmental toxicity study New Zealand White rabbits PMRA No. 3349191	Acceptable with limitations Maternal toxicity: ≥ 300 mg/kg bw/day: ↓ bwg GD 6 – 8 1000 mg/kg bw/day: ↓ bwg GD 26 – 29 and 6 – 29, ↓ fc GD 12 – 14 Developmental toxicity: No adverse findings up to 1000 mg/kg bw/day

Study type/Animal/PMRA No.	Study results
	Limitations: 8 does/dose; only external examinations of the fetuses were performed
Developmental gavage toxicity study New Zealand White rabbits PMRA No. 3349188, 3349189, 3349190	**Maternal toxicity:** **NOAEL** = 1000 mg/kg bw/day HDT **LOAEL** – undetermined **Developmental toxicity:** **NOAEL** = 1000 mg/kg bw/day HDT **LOAEL** – undetermined No evidence of sensitivity of the young No treatment-related malformations
Genotoxicity studies	
Ames test TA 1535, TA 1537, TA 98, TA 100, TA 102 of *S. typhimurium* PMRA No. 3349192	Negative ± metabolic activation Tested up to the limit dose
Ames test TA 1535, TA 1537, TA 98, TA 100, TA 102 of *S. typhimurium* PMRA No. 3349193	Negative ± metabolic activation Tested up to the limit dose
Gene mutation assay V79/HPRT PMRA No. 3349198	Negative ± metabolic activation Tested up to precipitating concentrations
Chromosome aberration test Human lymphocytes in vitro PMRA No. 3349202	Negative ± metabolic activation Tested up to precipitating concentrations
In vitro micronucleus test	Negative ± metabolic activation

Study type/Animal/PMRA No.	Study results
Human lymphocytes PMRA No. 3349206	Tested up to precipitating concentrations
In vitro micronucleus test Human lymphocytes PMRA No. 3349207	Negative ± metabolic activation Tested up to precipitating concentrations
In vivo micronucleus test NMRI mice PMRA No. 3349208	Negative Pretest 2000 mg/kg bw – bioavailability confirmed, ruffled fur (♂♀); ↓ spontaneous activity (♂) 1000 mg/kg bw - ruffled fur (♂♀) 2000 mg/kg bw – eyelid closure, ruffled fur (♂)
Immunotoxicity studies	
Immunotoxicity study Waiver rationale PMRA No. 3349254	Request to waive the conditionally required study was accepted based on the lack of signs of immunotoxicity in the BCS-CS55621 in the rest of database.
Neurotoxicity studies	
Acute gavage neurotoxicity study Han Wistar rats PMRA No. 3349252	NOAEL = 3000 mg/kg bw/day HDT (♂/♀) LOAEL – undetermined No evidence of neurotoxicity
Subchronic neurotoxicity study Waiver rationale PMRA No. 3349253	Request to waive the conditional requirement accepted based on lack of neurotoxicity for the BCS-CS55621in the rest of the database, including the acute neurotoxicity study.
Special Studies (non-guideline)	
Immature rat uterotrophic assay with vaginal opening assessments (gavage) Wistar rats (♀) PMRA No. 3349264	There were no effects on uterine weights or vaginal opening at 450 or 900 mg/kg bw/day The positive control studies adequately validated the study. **Negative**

Study type/Animal/PMRA No.	Study results
Weanling Hershberger assay with preputial separation assessments (gavage) Wistar rats (♂) PMRA No. 3349265	Acceptable with limitations Androgenic (10-day assay): 900 mg/kg bw/day - ↓ bw 4%, ↓ seminal vesicle wts (↓15%) Pubertal onset (30-day assay): 450 mg/kg bw/day - ↓ bw 5%, ↑ small/atrophic seminal vesicles (0, 1, 2) 900 mg/kg bw/day - ↓ bw (8%), ↓ tbw (9%), ↓ cowper's gland (18%), ↓ seminal vesicle wts (↓10%), ↓ ventral prostate wt (↓ 10%), ↓ liver wt (9%) Slight delay in preputial separation (<2 days) consistent with decreased body weight in prepubertal animals. Antiandrogenic (10 day assay): 450 mg/kg bw/day: ↑ seminal vesicle wts (↑ 11% and 13%), ↑ ventral prostate wts (↑ 11 and 17%) 900 mg/kg bw/day - ↓ bw Limitations: Assays performed with immature rats instead of castrated rats which interferes with any anti/androgenic properties of BCS-CS55621 as endogenous testosterone increases; authors did not compare CVs in the presence of a negative result, went below minimum group numbers in the high-dose group of the pubertal onset 30-day assay.
H295R steroidogenesis screen (in vitro) H295R cells PMRA No. 3349266	5.0 µM - ↓ progesterone (↓ 26%) with no effects on downstream hormones More than ±20% is considered an effect; however, a positive result is an increase in progesterone as opposed to a decrease. **Negative up to cytotoxic concentrations**
Metabolite studies - BCS-BP32808	
Acute oral toxicity study Wistar rats PMRA No. 3349164	LD_{50} = 175 mg/kg bw (CI 29-714) High acute oral toxicity Clinical signs: decreased activity, hunched posture, piloerection, incoordination and cold to touch

Study type/Animal/PMRA No.	Study results
28-day oral toxicity study with 14-day recovery (gavage) Han Wistar rats PMRA No. 3349177	NOAEL = 2 mg/kg bw/day (♂/♀) LOAEL = 5 mg/kg bw/day (♂/♀) Effects at the LOAEL ↓ bwg, ↓ high beam breaks (♂♀); ↑ piloerection and ↓ activity first day of treatment, ↓ motor activity wk 4 (high and low beam breaks), ↓ urea (♂); ↓ bw, ↓ creatinine, ↑ potassium (♀) Recovery was incomplete, but did occur
Ames test TA 1535, TA 1537, TA 98, TA 100, and TA 102 of S. typhimurium PMRA No. 3349196	**Positive ± metabolic activation** Induction of gene mutations in TA1535 with activation and TA100 ± metabolic activation of more than twofold compared to solvent and negative controls at ≥ 2500 µg/plate, but significantly less than positive controls.
Gene mutation assay V79/HPRT PMRA No. 3349199	Negative ± metabolic activation Tested up to cytotoxic concentrations
Chromosome aberration test Human lymphocytes PMRA No. 3349203	**Positive in absence of metabolic activation** Mutagenic in the absence of S9 mix in the 20hr exposure group in all tested groups (statistically significant and exceeded historical controls at low and high dose, but lower than positive controls)
In vivo micronucleus test NMRI mice PMRA No. 3349209	Negative Range-finding assay 25 mg/kg bw – hunched posture, partly closed eyes (with pale secretion or reddening), eyelid closure, ruffled fur, slightly reduced spontaneous activity (with aggravated breathing) ♂/♀ 50 mg/kg bw – leaning on cage wall, hunched posture, partly closed eyes, eyelid closure, lacrimation, ruffled fur, slightly reduced spontaneous activity ♂/♀ 125 mg/kg bw – hunched posture, abdominal position, partly closed eyes, eyelid closure, lacrimation, ruffled fur, slightly reduced spontaneous activity, apathy, increased activity, excitement, salivation, abdominal breathing, tumbling ♂/♀ - pre-test terminated

Study type/Animal/PMRA No.	Study results
	after 4 hours 500 mg/kg bw – leaning on cage wall, partly closed eyes, lacrimation, abdominal breathing, alternation between apathy and excitement, tumbling, tippy toe walk, strong salivation ♂/♀ – pre-test terminated after 1 hr Main study 5 mg/kg bw – partly closed eyes, ruffled fur, reduced spontaneous activity 10 mg/kg bw – partly closed eyes, ruffled fur, reduced spontaneous activity, soft feces 20 mg/kg bw – partly closed eyes (with encrustation), eyelid closure, ruffled fur, reduced spontaneous activity, reduced breathing
Metabolite studies – BCS-CC26101	
Ames test TA 1535, TA 1537, TA 98, TA 100, and TA 102 of S. typhimurium PMRA No. 3349194	Negative ± metabolic activation Tested up to the limit concentration
Gene mutation assay V79/HPRT PMRA No. 3349200	Negative ± metabolic activation Tested up to the limit concentration
In vitro micronucleus test Human lymphocytes PMRA No. 3349204	Negative ± metabolic activation Tested up to the limit concentration
Metabolites studies – BCS-CZ38260	
Ames test TA 1535, TA 1537, TA 98, TA 100, and TA 102 of S. typhimurium PMRA No. 3349195	Negative ± metabolic activation Tested up to the limit concentration
Gene mutation assay V79/HPRT	Negative ± metabolic activation Tested up to the limit concentration (10mM)

Study type/Animal/PMRA No.	Study results
PMRA No. 3349201	
In vitro micronucleus test Human lymphocytes PMRA No. 3349205	Negative ± metabolic activation Tested up to the limit concentration (10mM)
Metabolite studies – BCS-CU97237	
Ames test TA 1535, TA 1537, TA 98, TA 100, and TA 102 of S. typhimurium PMRA No. 3349197	Negative ± metabolic activation Tested up to a cytotoxic concentration

Table 6 Toxicity profile of end-use product(s) containing fluoxapiprolin

Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, effects observed in both sexes are presented first followed by sex-specific effects in males, then females, each separated by semi-colons.

Acute toxicity studies – BCS-CS55621 SC 20	
Acute oral toxicity (Up and Down procedure) Crl:WI Wistar rats PMRA No. 3349560	LD_{50} > 5000 mg/kg bw - ♂♀ Low acute oral toxicity Clinical signs of toxicity included hunched posture on Day 0
Acute dermal toxicity Crl:WI Wistar rats PMRA No. 3349561 DER	LD_{50} > 2000 mg/kg bw - ♀ Low acute dermal toxicity No clinical signs of toxicity
Acute inhalation toxicity Crl:WI Wistar rats PMRA No. 3349562	LC_{50} > 5.04 mg/L - ♂♀ Low acute inhalation toxicity Clinical signs of toxicity included laboured respiration, red-brown staining, and body weight loss Days 1–3
Eye irritation New Zealand White rabbits PMRA No. 3349563	$MIS_{(1hr)}$ = 0/110 $MAS_{(24\text{-}72hrs)}$ = 0/110 Non-irritating to the eye

Acute toxicity studies – BCS-CS55621 SC 20	
Dermal irritation New Zealand White rabbits PMRA No. 3349564	$MIS_{(1hr)}$ = 0/8 $MAS_{(24\text{-}72hrs)}$ = 0/8 Non-irritating to the skin
Dermal sensitization - LLNA CBA/CaOlaHsd mice PMRA No. 3349565	Positive Potential dermal sensitizer

Table 7 AHETF/PHED/NDETF unit exposure estimates for mixer/loaders and applicators handling end-use product (µg/kg a.i. handled)

Exposure scenario and PPE	Dermal	Inhalation[1]
PPE: Single layer, CR gloves		
Mixer/loader AHETF estimates		
Liquid formulation, open mix/load	58.50	0.63
Applicator AHETF estimates		
Groundboom, open cab	25.40	1.68
Airblast, open cab	3769.30	9.08
Aerial (pilot), closed cockpit	2.67	0.00969
Mixer/loader/applicator PHED estimates		
HH-Backpack (Scenario 23a)	5445.85	62.10
HH-MPHG (Scenario 24a)	5585.49	151.00
HH-MPHW (Scenario 21a)	943.37	45.20
PPE: CR coveralls, CR gloves, respirator, CR hat		
Applicator NDETF estimates		
HH – AB/MB	32561	3940

CR = Chemical-Resistant, HH = Handheld, HH-MPHG = Mechanically Pressurized Handgun, HH-MPHW = Manually Pressurized Handwand, HH-AB/MB = Airblast/Mistblower

[1] Light inhalation rate for all equipment except for backpack or handheld airblast/mistblower, which use the moderate inhalation rate.

Table 8 Occupational mixer/loader/applicator exposure and risk assessment for fluoxapiprolin

Application method	Application rate	ATPD or AHPD	Exposure (µg/kg bw/day)[1]		MOE	
			Dermal	Inhalation	Dermal[2]	Inhalation[3]
Single Layer, CR Gloves (MLA)						
HH-Backpack – Grapes	0.04 g/L	150 L	0.41	0.005	2.45E+06	2.13E+07
HH-MPHG – Grapes	0.04 g/L	3800	10.6	0.29	9.42E+04	3.45E+05

Application method	Application rate	ATPD or AHPD	Exposure (µg/kg bw/day)[1]		MOE	
			Dermal	Inhalation	Dermal[2]	Inhalation[3]
		L				
HH-MPHW – Grapes	0.04 g/L	150 L	0.07	0.003	1.41E+07	2.92E+07
HH-Backpack – Vegetables	0.2 g/L	150 L	2.04	0.02	4.90E+05	4.25E+06
HH-MPHG – Vegetables	0.2 g/L	3800 L	53.1	1.43	1.88E+04	6.90E+04
HH-MPHW – Vegetables	0.2 g/L	150 L	0.35	0.02	2.83E+06	5.84E+06
Aerial (A) – Potato	0.02 kg/ha	400 ha	0.27	0.0010	3.75E+06	1.02E+08
Aerial (M/L) – Potato	0.02 kg/ha	400 ha	5.85	0.06	1.71E+05	1.57E+06
Airblast (M/L/A) – Grapes	0.02 kg/ha	20 ha	19.1	0.05	5.22E+04	2.04E+06
Groundboom (M/L/A), large field crops, custom applicator	0.02 kg/ha	360 ha	7.551	0.208	1.32E+05	4.76E+05
Groundboom (M/L/A), large field crops, farmer	0.02 kg/ha	107 ha	2.24	0.06	4.46E+05	1.60E+06
Groundboom (M/L/A), small field crops	0.02 kg/ha	26 ha	0.55	0.02	1.83E+06	6.59E+06
Single layer, CR gloves (M/L); CR coveralls, CR gloves, Respirator and CR hat (A)						
HH-AB/MB - Grapes	0.04 g/L	150 L	2.45	0.30	4.09E+05	3.35E+05

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

1 Exposure = (Unit exposure × ATPD × Rate) / (80 kg bw × 1000 µg/mg)

2 Based on dermal NOAEL of 1000 mg/kg bw/day; Target MOE = 100 (see Table 3)

3 Based on an inhalation NOAEL of 99 mg/kg bw/day; Target MOE = 300 (see Table 3)

Table 9 Postapplication worker exposure and risk estimate for fluoxapiprolin on day 0 after the last application

Crops/Crop Groups	NAPS	RTI	Activity	TC[1] (cm²/hr)	Peak DFR	Day 0 Estimates		REI[4] (days)
						Exp[2]	MOE[3]	
Crop Group 5-13	3	7	Hand Harvesting	5150	0.09	44.0	22700	0.5
Crop Group 3-07	3	7	Hand Weeding	4400	0.09	37.6	26600	0.5
Crop Group 9; Crop Group 8-09A; Group 8-09B; Crop Group 4-13; Crop Subgroup 22B; Potato	3	7	Irrigation (hand set)	1750	0.09	14.9	66900	0.5
Grapes	2	10	Girdling,	19300	0.07	130	7680	0.5

Crops/Crop Groups	NAPS	RTI	Activity	TC[1] (cm^2/hr)	Peak DFR	Day 0 Estimates		REI[4] (days)
						Exp[2]	MOE[3]	
			Turning					

NAPS = Number of Applications per Season, RTI = retreatment interval (days), TC = Transfer Coefficient, DFR = Dislodgeable Foliar Residue, Peak DFR = Day 0 DFR (ug/cm^2), Exp = Exposure (ug/kg bw/day), MOE = Margin of Exposure, REI = Restricted-Entry Interval

1 Transfer coefficients obtained from the ARTF

2 Exposure (µg/kg bw/day) = (Peak DFR [µg/cm^2] × TC [cm^2/hr] × 8 hours) / (80 kg bw)

3 MOE = NOAEL ÷ (Exposure (µg/kg bw/day) × Conversion Factor (mg/1000 µg)); Based on a NOAEL of 1000 mg/kg bw/day, Target MOE = 100 (see Table 3)

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

Table 10 Major fate inputs for the modelling EECs in drinking water

Fate parameter	Parent Group (fluoxapiprolin + BCS-CS55621-4-OH-piperidine) [formation fraction]	BCS-CS55621-pyrazole acetic acid [formation fraction]	BCS-CS55621-lactam [formation fraction]	BCS-CS55621-BDM-pyrazole [formation fraction]
K_d (L/kg)	79 (lower of the two values for the substances in the parent group, 20th percentile of 5 soils)	0.034 (20th percentile of 4 soils)	34 (20th percentile of 4 soils)	0.13 (20th percentile of 5 values)
Water half-life (days at 20°C)[1]	20 (shorter of 2 values)	146 [1] (longer of 2 values)	155 [0.78] (longer of 2 values)	Stable (no data)
Sediment half-life (days at 20°C)[2]	110 (shorter of 2 values)	1230 [0.51] (single value)	Stable [0] (single value)	Stable (no data)
Photolysis half-life	Stable (single value)	Stable (single value)	Stable (single value)	Stable (no data)
Hydrolysis	Stable (single value)	Stable (single value)	Stable (single value)	Stable (no data)
Soil half-life (days at 20°C)	17 (mean of 6 values) for surface water	63 [0.63] (90% confidence bound on the mean of 6 values) for surface water	Stable [0.48] (no transformation in 2 of 6 experiments) for surface water	14.6 (single value)

[1] Aquatic whole system

[2] Anaerobic aquatic whole system

Table 11 Half-lives and formation fractions for groundwater from the six soil experiments

Soil identifier	Parent Group (fluoxapiprolin + BCS-CS55621-4-OH-piperidine) [formation fraction]	BCS-CS55621-pyrazole acetic acid [formation fraction]	BCS-CS55621-lactam [formation fraction]	BCS-CS55621-BDM-pyrazole [formation fraction]
PCA	27 days	15 days [0.45]	531 days [0.088]	-
LNE	24 days	120 days [0.37]	Stable [0.81]	14.6 days (16 g/ha)[1]
HN	12 days	22 days [0.51]	230 days [0.20]	-
AX	14 days	26 days [0.75]	285 days [0.30]	-
HH	9 days	25 days [0.70]	254 days [0.34]	-
DD	15 days	26 days [0.44]	Stable [0.24]	-

[1] BCS-CS55621-BDM-pyrazole was applied as parent and was modelled at 16 g/ha, adjusted by molecular weight.

Table 12 Level 1 estimated environmental concentrations of a combined residue of fluoxapiprolin, BCS-CS55621-lactam, BCS-CS55621-pyrazole acetic acid, and BCS-CS55621-4-OH-piperidine in potential sources of drinking water as the parent equivalent

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)		
	Peak[1]	Post-breakthrough Average[2]	Daily[3]	Yearly[4]	Overall[5]
60 g fluoxapiprolin/ha per year	16	14	1.8	0.84	0.71

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

Table 13 Level 1 estimated environmental concentrations of BCS-CS55621-BDM-pyrazole in potential sources of drinking water as the parent equivalent

Use pattern	Groundwater (µg a.i./L)		Surface water (µg a.i./L)		
	Peak[1]	Post-breakthrough average[2]	Daily[3]	Yearly[4]	Overall[5]
16 g BCS-CS55621-BDM-pyrazole/ha per year (equivalent to 60 g fluoxapiprolin/ha per year)	1.4	0.95	1.4	0.24	0.14

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

Table 14 Integrated food residue chemistry summary

Nature of the residue in laying hen		PMRA No. 3349150; 3349151
Species and numbers	Six laying hens per radiolabel (*Gallus gallus Domesticus*)	
Radiolabel position	[Phenyl-U^{14}C] (specific activity: 4.10 MBq/mg) [Pyrazole-4-^{14}C] (specific activity: 3.59 MBq/mg)	
Average dose	[Phenyl-U-^{14}C]: 17.78 mg a.i./kg dry feed [Pyrazole-4-^{14}C]: 17.74 mg a.i./kg dry feed	
Treatment regimen	Once daily by gavage using syringe	
Study period	14 consecutive days	
Collection time	Eggs and excreta once daily after administration	
Tissues collected	Muscle (leg, thorax), subcutaneous fat, skin (without subcutaneous fat), liver (without gall bladder) and kidneys	
Interval from last dose to sacrifice	6 hours	
Plateau of residues in eggs	Approximately 7 days after the first administration	
Extraction solvents	Acetonitrile/water (8/2; v/v)	
Exhaustive extraction	Solids of eggs and liver after conventional extraction were exhaustively extracted with acetonitrile/water (4/1; v/v and 1/1; v/v, respectively) using microwave assistance.	
Matrices	**[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]**	
	Percentage of administered dose	**TRRs (ppm)**
Liver	0.04–0.05	0.212–0.250
Kidneys	<0.01	0.068–0.076
Eggs from ovary/oviduct	0.01	0.101–0.104
Composite muscle	0.01–0.03	0.005–0.010

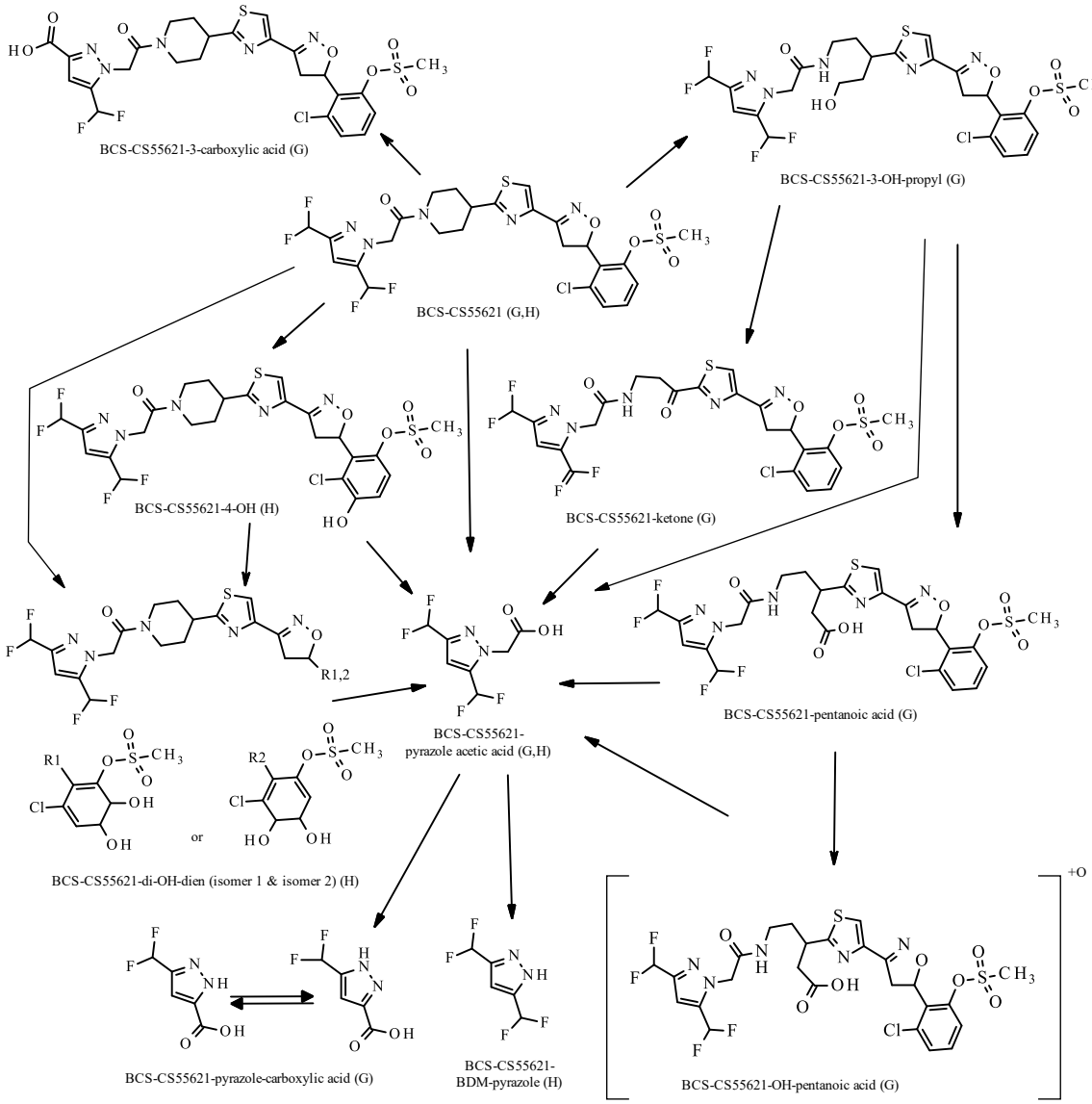
Composite skin without fat	<0.01–0.01	0.017–0.025
Composite fat	0.02	0.018–0.027
Total excreta	95–97	-
Summary of major identified metabolites in hen matrices		
Radiolabel position	**[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]**	
Composite fat	Fluoxapiprolin; fluoxapiprolin-BDM-pyrazole; fluoxapiprolin-pyrazole-acetic acid	
Composite muscle	Fluoxapiprolin; fluoxapiprolin-pyrazole-acetic acid	
Liver	Fluoxapiprolin-4-OH; fluoxapiprolin-pyrazole-acetic acid	
Pooled Eggs	Fluoxapiprolin; fluoxapiprolin-pyrazole-acetic acid	

Nature of the residue in lactating goat	**PMRA No. 3349152; 3349153**
Species and numbers	One lactating goat per radiolabel (*Capra hircus*)
Radiolabel position	[Phenyl-U-^{14}C]:(specific activity: 4.87 MBq/mg); [Pyrazole-4-^{14}C]:(specific activity: 3.59 MBq/mg)
Average dose	[Phenyl-U-^{14}C]: 23.86 mg a.i./kg dry feed; [Pyrazole-4-^{14}C]: 24.23 mg a.i./kg dry feed
Treatment regimen	Once daily orally by gelatin capsule
Study period	5 consecutive days
Collection time	Milk: 2/day (morning and evening); Excreta: 1/day
Tissues collected	Composite muscle (loin, round), composite fat (perirenal, omental), liver (without gall bladder), kidneys and milk
Interval from last dose to sacrifice	6 hours
Plateau of residues in milk	Could not be determined based on the limited sampling.
Extraction solvents	Acetonitrile/water (8:2; v/v)
Exhaustive extractions	Solids of kidney and liver remaining after conventional extraction were exhaustively extracted with mixtures of acetonitrile/water (1/1; v/v) using microwave assistance.

Matrices	**[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]**	
	Percentage of administered dose	**TRRs (ppm)**
Pooled Milk (Day 0-102 hours)	0.04–0.07	0.009–0.010
Liver	0.44–0.45	0.898–0.928
Kidneys	<0.01–0.01	0.042–0.076
Composite Fat	0.03	0.011–0.015
Composite Muscle	0.02–0.05	0.004–0.008
Total excreted	60-64	-
Summary of major identified metabolites in goat matrices		
Radiolabel position	**[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]**	
Composite fat	Fluoxapiprolin; fluoxapiprolin-pyrazole-acetic acid	
Kidneys	Fluoxapiprolin; fluoxapiprolin-pyrazole-carboxylic acid; fluoxapiprolin-pyrazole-acetic acid	
Liver	Fluoxapiprolin; fluoxapiprolin-pyrazole-carboxylic acid;	

	fluoxapiprolin-pyrazole-acetic acid
Whole milk	Fluoxapiprolin; fluoxapiprolin-pentanoic acid; fluoxapiprolin-pyrazole-acetic acid

Proposed metabolic scheme in livestock



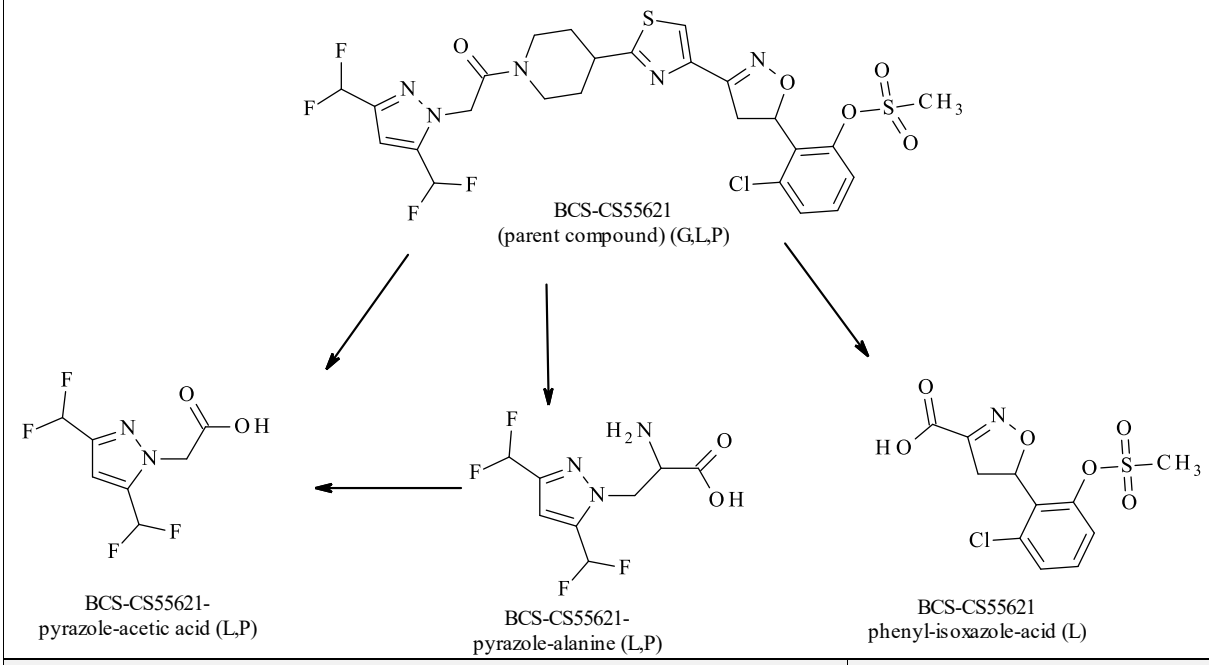
Nature of the residue in grapes, lettuce, potatoes			**PMRA No. 3349154/3349155 PMRA No. 3349156/3349158 PMRA No. 3349159/3349160**
Radiolabel position	[Phenyl-U-^{14}C]:(specific activity: 5.18 MBq/mg); [Pyrazole-4-^{14}C]:(specific activity: 3.59 MBq/mg)		
Test Site	In individual pots in greenhouse		
Crops/Variety	Grapes/ *Vitis vinifera* cv. Mueller-	Lettuce/ *Lactuca sativa L.* var.	Potatoes/ *Solanum tuberosum L.*

	Thurgau	*capitata* "Susana"	cv. Cilena
Total Rate (g a.i./ha)	60	Immature: 20 Mature: 60	60
Formulation	Emulsifiable concentrate (EC) formulation of fluoxapiprolin (guarantee: 20 g/L)		
Treatment	BBCH 16 (5–6th true leaves unfolded), BBCH 65 (30–50% flower heads fallen), and BBCH 85 (softening of berries)	BBCH 15 (5th true leaf unfolded); BBCH 42–43 (20–30% of the expected head size reached); BBCH 47–48 (70–80% of the expected head size reached)	BBCH 13-15 (3rd leaf main stem unfolded; > 4cm); BBCH 61 (10% of flowers in the first inflorescence open); and BBCH 93-95 (most of the leaves yellowish)
Preharvest interval (days)	14	Immature: 26 after 1st application; Mature: 7 after 3rd application	7
Extraction solvents	Acetonitrile/water (8:2; v/v)	Acetonitrile/water (8:2; v/v)	Tubers: Acetonitrile and acetonitrile/water (4:1, v/v)
			Tops: Acetonitrile/water (4:1; v/v)

Matrices	**PHI (days)**	**[Phenyl-U-^{14}C]/[Pyrazole-4-^{14}C] TRR (ppm)**
Grapes (surface-washed)	14	0.107–0.122
Grapes (non-washed)		0.145–0.149
Grape leaves		6.979–11.293
Immature head lettuce	26 after 1st application	0.043–0.045
Mature head lettuce	7	0.788–0.845
Potato tubers	7	0.026
Potato tops		7.425–11.525

Summary of major identified metabolites in plant matrices	
Radiolabel position	**[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]**
Surface washed grapes	Fluoxapiprolin
Non-washed grapes	Fluoxapiprolin
Grape leaves	Fluoxapiprolin
Immature lettuce	Fluoxapiprolin Fluoxapiprolin-phenyl-isoxazole acid Fluoxapiprolin-pyrazole-alanine Fluoxapiprolin-pyrazole-acetic acid
Mature head lettuce	Fluoxapiprolin
Potato tops	Fluoxapiprolin
Potato tubers	Fluoxapiprolin-pyrazole-alanine Fluoxapiprolin-pyrazole-acetic acid

Proposed Metabolic Scheme in Plants



Freezer storage stability in plant matrices			**PMRA No. 3349593**	
Tested matrices	**Analytes**	**Tested intervals (days)**	**Temperature (°C)**	**Category**
Tomatoes	Fluoxapiprolin	0, 91, 189, 365, 656, 740	≤ -18	High-water
Potatoes		0, 98, 185, 364, 658, 738		High-starch
Grapes		0, 92, 187, 362, 645, 740		High-acid
Sunflower seeds		0, 185, 366, 564, 731		High-oil
Dry field pea seeds		0, 184, 367, 567, 734		**High-protein**

Crop field trials and residue decline on potatoes, CG3-07, CG4-13, CG5-13, CG8-09, CG9, CSG13-07G, CSG22B, grapes	**PMRA No. 3349605-3349608; 3349610-3349612; 3349616; 3349619**

Crop field trials were conducted in North American growing regions during 2019-2021 seasons. The number and geographic distribution of trials were generally in accordance with Health Canada's SPN2017-02. Independence of trials was also assessed.

Fluoxapiprolin 20 SC was applied at rates ranging from 13–21 g a.i./ha for a maximum seasonal rate of 62 g a.i./ha., except for grapes for which the seasonal rate was 41 g a.i./ha (using concentrated and/or dilute spray volumes). Residue decline data show that residues of fluoxapiprolin either decreased or remained relatively unchanged with increasing preharvest intervals (PHIs). Adequate storage stability data are available on diverse crop types to support the storage intervals of the crop field trials. Samples were analyzed using a validated analytical method

Crop	Total application rate (g a.i/.ha/season)	PHI (days)	Fluoxapiprolin residue levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SDEV
Potatoes	59-62	5–7	25	<0.010	<0.010	<0.010	<0.010	0
Bulb onions	60-61	1–2	12	<0.010	0.022	<0.010	0.011	0.003
Green onions	60-62	1–3	5	0.025	0.750	0.263	0.379	0.331
Head lettuce	59-62	1–10	13	0.043	0.435	0.233	0.246	0.129
Leaf lettuce	59-62	1–3	14	0.201	1.458	0.750	0.821	0.393
Mustard greens	60-61	1–3	8	0.646	1.829	1.516	1.362	0.446
Spinach	60-62	1–9	11	0.840	3.874	1.555	1.745	0.857
Broccoli	59-61	1–3, 10	12	0.035	0.193	0.118	0.123	0.055
Cauliflower	59-61	1–10	11	<0.010	0.141	0.095	0.077	0.055
Cabbages	59-62	1–10	12	0.030	0.447	0.227	0.206	0.138
Bell peppers	57-62	1–3	12	<0.010	0.032	0.023	0.022	0.008
Non-bell peppers	57-60	1–3	4	<0.010	0.033	0.015	0.018	0.011
Tomatoes	57-62	1–7	27	<0.010	0.036	0.019	0.020	0.008
Cucumbers	59-62	1–9	11	<0.010	0.042	<0.010	0.014	0.010
Summer squash	59-61	1–2	12	<0.010	0.026	0.011	0.014	0.006
Muskmelons	59-62	1–10	13	<0.010	0.045	0.016	0.022	0.012
Grapes (dilute spray)	40-41	12–14, 21, 28, 35	15	0.026	0.144	0.064	0.069	0.029
Celery	60-61	1–10	8	0.135	0.738	0.550	0.478	0.235

n = number of independent trials.
For computation, values <LOQ are assumed to be at the LOQ of 0.01 ppm.

Processed food and feed - Crop | **PMRA No. 3349624**

Processing studies were conducted on tomatoes in 2017 in North American growing regions using Fluoxapiprolin 20SC at 230 g a.i./ha (~fourfold of maximum seasonal use rate). Processing studies were also conducted on potatoes and grapes in European regions using Fluoxapiprolin 20SC applied to potatoes at 300 g a.i./ha (fivefold of maximum seasonal use rate) and to wine grapes and table grapes at 200 g a.i./ha (fivefold of maximum seasonal use rate). 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.

Note: Fluoxapiprolin residues were all <LOQ (<0.01 ppm) in potato tuber and all processed commodities, therefore, processing factors could not be calculated.

RAC	Processed fractions	$HAFT_{[RAC]}$ (ppm)	Mean/Median processing factor of fluoxapiprolin	Anticipated residues of fluoxapiprolin (ppm)
Grapes	Raisins	0.144	3.3	0.475
	Juice		<0.04	0.006

	Wine at bottling		<0.04	0.006
Tomatoes	Dried tomatoes	0.036	5.3	0.191
	Juice		0.1	0.004
	Paste		0.4	0.014
	Purée		0.2	0.007

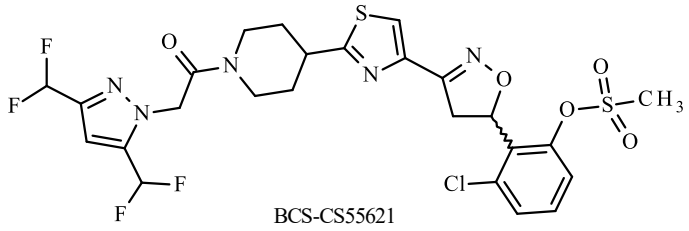
Confined accumulation in rotational crops – Tier I Study Wheat, Swiss chard, Turnips			**PMRA No. 3349622; 3349623**
Radiolabel position	[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]		
Specific activity	Phenyl: 5.18 MBq/mg (applied: 25.4 MBq/m^2); Pyrazole: 3.59 MBq/mg (applied: 21.5 MBq/m^2)		
Test site	In individual pots in greenhouses		
Soil type	Sandy loam		
Treatment	Bare soil was treated at 51–61 g a.i./ha, and aged for 30, 154 and 260–271 days.		
Formulation	Emulsifiable concentrate (EC) formulation of fluoxapiprolin (guarantee: 25 g/L)		
Extraction solvents	Acetonitrile/water (8/2; v/v)		
Radiolabel position	[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]		
Matrices	1st Rotation (30-day PBI)	2nd Rotation (154-day PBI)	3rd Rotation (260-271-day PBI)
Wheat forage	0.004–0.032	0.007–0.026	0.003–0.014
Wheat hay	0.019–0.121	0.011–0.056	0.006–0.039
Wheat straw	0.022–0.186	0.008–0.063	0.008–0.068
Wheat grain	0.012–0.034	0.004–0.013	0.004–0.011
Swiss chard (immature)	0.003–0.021	0.004–0.010	0.002–0.006
Swiss chard (at maturity)	0.004–0.030	0.004–0.016	0.003–0.008
Turnip roots	0.001–0.026	0.001–0.015	<0.001–0.009
Turnip greens	0.003–0.138	0.005–0.058	0.002–0.036

Summary of major identified metabolites in rotated crops			
Radiolabel	[Phenyl-U-^{14}C], [Pyrazole-4-^{14}C]		
Plantback Intervals (PBI)	1st Rotation (30-day PBI)	2nd Rotation (154-day PBI)	3rd Rotation (260–271-day PBI)
Spring wheat grain	Fluoxapiprolin-phenyl-isoxazole acid Fluoxapiprolin-pyrazole-acetic acid	Fluoxapiprolin-pyrazole-alanine Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-lactic acid	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid

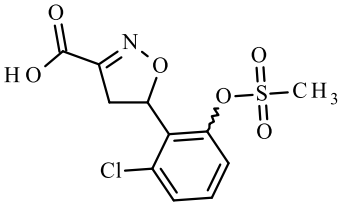
Spring wheat forage	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid Fluoxapiprolin-pyrazole-carboxylic acid	Fluoxapiprolin-pyrazole-methylsulfinyl acid Fluoxapiprolin-pyrazole-carboxylic acid	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid Fluoxapiprolin-pyrazole-carboxylic acid
Spring wheat hay	Fluoxapiprolin-phenyl-isoxazole acid Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid	Fluoxapiprolin-phenyl-isoxazole acid Fluoxapiprolin-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid
Spring wheat straw	Fluoxapiprolin-phenyl-isoxazole acid Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid	Fluoxapiprolin-phenyl-isoxazole acid Fluoxapiprolin-pyrazole-methylsulfinyl acid	Fluoxapiprolin-pyrazole-methylsulfinyl acid
Swiss chard (immature)	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-alanine	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid Fluoxapiprolin-pyrazole-alanine-oxopropanoic acid Fluoxapiprolin-pyrazole-lactic acid	None
Swiss chard (mature)	Fluoxapiprolin-pyrazole-acetic acid	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-methylsulfinyl acid Fluoxapiprolin-pyrazole-alanine-oxopropanoic acid Fluoxapiprolin-pyrazole-lactic acid	None
Turnip roots	Fluoxapiprolin-pyrazole-alanine	Fluoxapiprolin-pyrazole-alanine	Fluoxapiprolin-pyrazole-alanine

Turnip greens	Fluoxapiprolin-pyrazole-acetic acid Fluoxapiprolin-pyrazole-alanine Fluoxapiprolin-alanine-oxopropanoic acid	Fluoxapiprolin-pyrazole-alanine Fluoxapiprolin-alanine-oxopropanoic acid	Fluoxapiprolin-pyrazole-alanine Fluoxapiprolin-alanine-oxopropanoic acid

Proposed metabolic scheme in rotational crops
[Phenyl-U-^{14}C]

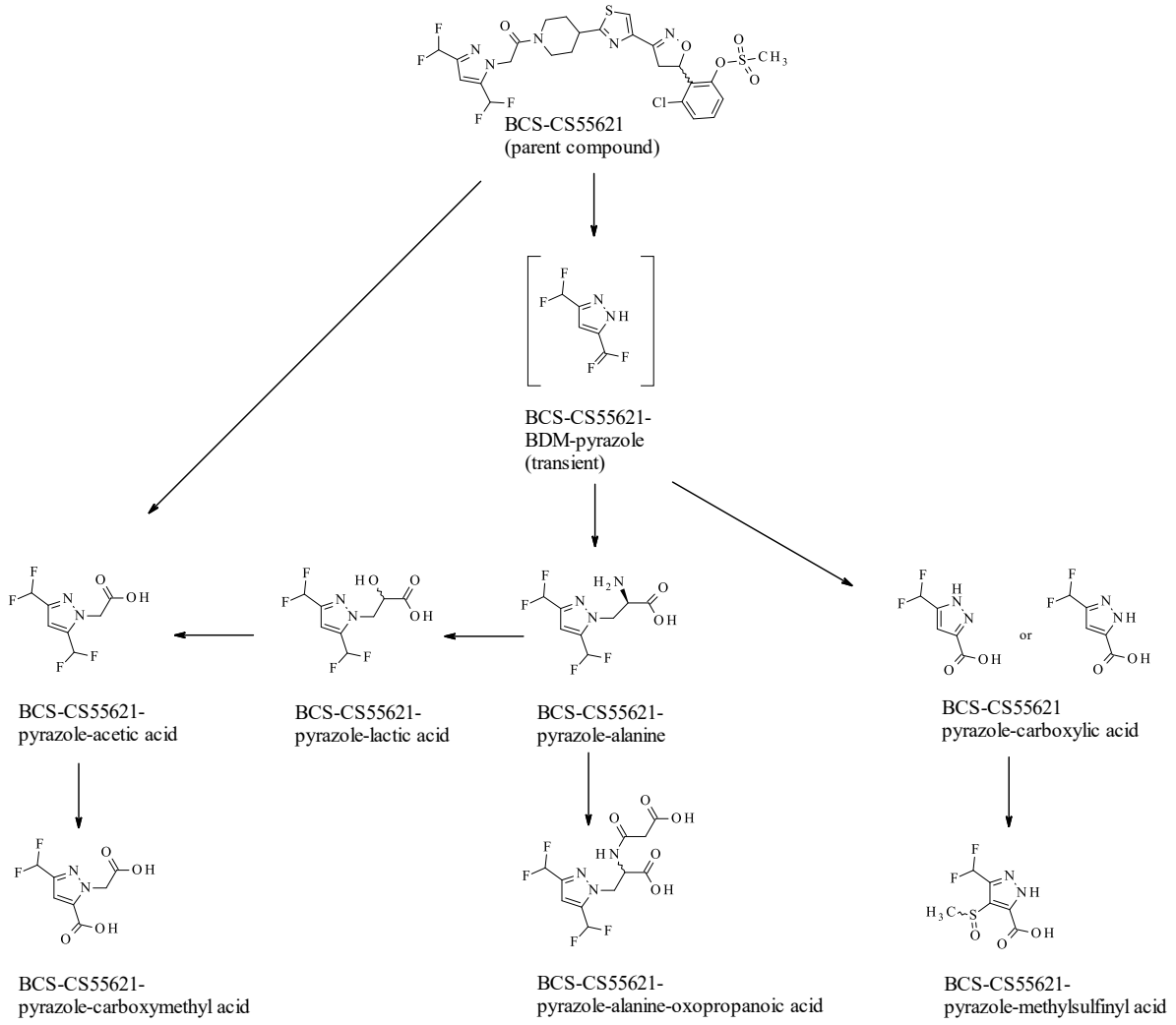


BCS-CS55621



BCS-CS55621-phenyl-isoxazole acid

[Pyrazole-4-^{14}C]



Residue data in rotational crops – Tier II study	**PMRA No. 3349597; 3349598; 3349599**
Nine trials (three each for soybeans, turnips, and wheat) were conducted during the 2019–2020 growing seasons in North American growing regions. Three broadcast applications were made to bare soil with Fluoxapiprolin 20 SC at a rate of 20–21 g a.i./ha/application, with retreatment intervals of 5 to 7 days, for a maximum of 61 g a.i./ha. Rotational crops were planted at three different plantback intervals of 25-30 days, 111–119 days, and 344–392 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
Soybean forage	60–61	28	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	60	113–117	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	59–61	352–364	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Soybean hay	60–61	28	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	60	113–117	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	59–61	352–364	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Soybean seed	60–61	28	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	60	113–117	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	59–61	352–364	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Wheat forage	59–61	25–30	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		112–115	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		344–356	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Wheat hay	59–61	25–30	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		112–115	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		344–356	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Wheat straw	59–61	25–30	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		112–115	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		344–356	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Wheat grain	59–61	25–30	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
		112–115	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0

		344–356	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Turnip roots	60–61	25–29	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	59–60	111–119	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	60–61	349–392	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
Turnip greens	60–61	25–29	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	59–60	111–119	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0
	60–61	349–392	Fluoxapiprolin	3	<0.010	<0.010	<0.010	<0.010	0

Residue data in rotational wheat - Tier II study **PMRA No. 3703295**

Based on a cursory review of this field rotational study, where wheat was planted 30 days following application of fluoxapiprolin to bare soil at a rate of 60 g a.i./ha, residues of fluoxapiprolin were <LOQ in wheat forage, hay, straw and grain. However, measurable residues of specific fluoxapiprolin metabolites were observed in forage, hay and straw. More specifically, the HAFT residues of the metabolite fluoxapiprolin-pyrazole-methyl-sulfinyl acid were 0.012 ppm in wheat forage, 0.024 ppm in wheat hay and 0.015 ppm in wheat straw. The HAFT residues of the metabolite fluoxapiprolin-pyrazole-alanine were 0.010 ppm in wheat straw only. HAFT residues of fluoxapiprolin-pyrazole-acetic acid were 0.010 ppm in wheat forage and 0.011 ppm in wheat hay. Residues of fluoxapiprolin metabolites were all <LOQ in wheat grain.

Therefore, a PBI of 115 days, based on the Tier II studies summarized above (PMRA No. 3349597; 3349598; 3349599), is recommended to ensure there is no uptake of quantifiable residues of the fluoxapiprolin metabolites in wheat forage, hay, straw and grain. In turn, no measurable residues of any fluoxapiprolin metabolites would be expected in animal matrices when livestock are fed treated feed items derived from wheat planted as a secondary crop.

Residue data in rotational crops - Tier III study **PMRA No. 3349600**

Ten field trials were conducted on during the 2020–2021 growing seasons in North American growing regions. Three broadcast applications were made to bare soil with Fluoxapiprolin 20 SC at a rate of 20–21 g a.i./ha/application, with retreatment intervals of 5 to 8 days, for a maximum of 61 g a.i./ha/season. Strawberries were planted 23–30 days following application to bare soil. 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)**	**Analyte**	**Residue levels (ppm)**					
				n	**LAFT**	**HAFT**	**Median**	**Mean**	**SDEV**

Strawberries	60–61	23–30	Fluoxapiprolin	10	<0.010	<0.010	<0.010	<0.010	0
n = number of independent trials.									
Based on the results of the field accumulation study, a plantback interval of 30 days for strawberries, 115 days for small grain cereals, 12 months for all crops not listed on the label and a rotational restriction for root vegetables (Crop Subgroup 1A) are supported.									

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

Plant studies			
Residue definition for enforcement			
Primary crops (grapes, lettuce, potatoes) **Rotational crops (turnips, Swiss chard, wheat)**		Fluoxapiprolin	
Residue definition for risk assessment			
Primary crops (grapes, lettuce, potatoes)		Fluoxapiprolin, Fluoxapiprolin-BDM-pyrazole (Each assessed separately)	
Rotational crops (turnips, Swiss chard, wheat)		Fluoxapiprolin and fluoxapiprolin-pyrazole-alanine, expressed as parent equivalents	
Metabolic profile in diverse crops		The metabolic profile in lettuce, potatoes and rotational crops was similar. There was no degradation of the fluoxapiprolin observed in grapes.	
Animal studies			
Animals		**Ruminant and poultry**	
Residue definition for enforcement		Fluoxapiprolin	
Residue definition for risk assessment			
Metabolic profile in animals (goat, hen, rat)		The metabolism of fluoxapiprolin is more extensive in lactating goats in comparison to the laying hens and rats.	
Fat soluble residue		Yes	
Dietary risk from food and drinking water			
Fluoxapiprolin	**Population**	**Estimated risk percentage of acute reference dose (ARfD)**	
		Food only	**Food and drinking water**
Basic acute dietary exposure analysis **ARfD = 1 mg/kg bw** **Estimated peak drinking water concentration = 0.016 ppm**	Females 13–49 years	0.56	0.61

	Population	Estimated risk percentage of acceptable daily intake (ADI)	
		Food only	**Food and drinking water**
Basic chronic dietary exposure analysis **ADI = 1 mg/kg bw/day** **Estimated post-breakthrough average drinking water concentration = 0.014 ppm**	Total population	0.1	0.2
	All infants <1 year	0.1	0.2
	Children 1–2 years	0.3	0.3
	Children 3–5 years	0.2	0.2
	Children 6–12 years	0.1	0.1
	Youth 13–19 years	0.1	0.1
	Adults 20–49 years	0.1	0.2
	Adults 50+ years	0.1	0.2
Fluoxapiprolin-bdm-pyrazole	**Population**	**Estimated risk percentage of acceptable daily intake (ADI)**	
		Food only	**Food and drinking water**
Intermediate chronic dietary exposure analysis **ADI = 0.0007 mg/kg bw/day** **Estimated post-breakthrough average drinking water concentration = 0.00095 ppm**	Total population	6.3	9.0
	All Infants	6.8	17.1
	Children 1–2 years	18.1	21.8
	Children 3–5 years	14.5	17.6
	Children 6–12 years	8.4	10.6
	Youth 13–19 years	5.0	7.0
	Adults 20–49 years	5.3	8.0
	Adults 50+ years	5.2	7.9

Table 16 Fate and behaviour in the environment

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
Abiotic transformation						
Hydrolysis	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled pH 4, and 7 at 50°C for 30 d pH 9 at 25, 35 and 50 °C for 30 d	Stable to hydrolysis at pH 4, and 7 at 50°C; At pH 9: stable at 25°C, DT_{50}/t_R = 202.1 d at 35°C, DT_{50}/t_R = 28.51 d at 50°C	**Major:** BCS-CS55621-desmesyl (BCS-CS15122), only at pH 9 and 50 °C **Minor:** none	Hydrolysis is not expected to be an important route of dissipation for fluoxapiprolin in the environment	Acceptable	3349332
Phototransformation on soil	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled loamy sand, pH 5.9, organic carbon 1.5% 20 ± 1°C, 55 ± 5% MWHC Continuous irradiation, 580 W/m^2 in 300-800 nm	Corrected DT_{50}/t_R = 114.8 d (SFO) DT_{50}/t_R equivalent under natural summer sunlight at Edmonton: 419 d	**Major:** none **Minor:** multiple unidentified (total max 15.1% AR, none > 4.7% AR) NER 3.8% AR CO_2 and VOC < 0.3% AR	Phototransformation on soil is not expected to be an important route of dissipation for fluoxapiprolin in the environment.	Acceptable	3349334

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled sandy loam, pH 5.6, organic carbon 1.3% 20 ± 1°C, 55 ± 5% MWHC Continuous irradiation, 580 W/m^2 in 300-800 nm	Stable (DT_{50}/t_R were about the same in irradiated and dark control tests)	**Major:** none **Minor:** BCS-CS55621-4-OH-piperidine (max 6.6% AR), other unidentified (total 8.3% AR, none > 5.4% AR) NER 2.6% AR CO_2 and VOC ≤ 0.1% AR		Acceptable	3349335
Phototransformation in water	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled Sterile pH 7 buffer, 25±2°C, continuous irradiation, 505 W/m^2 in 300-800 nm	Corrected DT_{50}/t_R = 40.8 d (SFO) DT_{50}/t_R equivalent under natural summer sunlight at Edmonton: 130 d	**Major:** none **Minor:** five unidentified (total max 17.4% AR, none > 4.3% AR except one single detect at 9.4% AR) CO_2 2.6% AR	Phototransformation in water is not expected to be an important route of dissipation for fluoxapiprolin in the environment	Acceptable	3349336
	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled	Corrected DT_{50}/t_R = 37.1 d (SFO)	**Major:** none **Minor:** multiple unidentified		Acceptable	3349338

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	Sterile pH 7 buffer, 25±2°C, continuous irradiation, 507 W/m^2 in 300-800 nm	DT_{50}/t_R equivalent under natural summer sunlight at Edmonton: 118.7 d	(total max 32.5% AR, none > 7.2% AR) CO_2 < 0.1% AR			
Phototransformation in air	Estimated using AOPWIN (version 1.92)	Not determined. The AOPWIN (v1.92) model is not suited for predicting the atmospheric half-life of fluoxapiprolin given the large fraction expected to be sorbed to airborne particles.	NA		Acceptable with limitations	3349340
Biotransformation						
Biotransformation of the parent in aerobic soil	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled 2 US soils: PCA: Sandy loam,	**PCA:** DT_{50}/t_R = 64.2/83.5 d (DFOP) **LNE:** DT_{50}/t_R =	**Major:** BCS-DA63612, BCS-DC21250 **Minor:** BCS-CY96288, BCS-DG91934	Fluoxapiprolin is non-persistent to moderately persistent in aerobic conditions, depending on soil	Acceptable	3349341

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	pH 7.2, OC 0.69% LNE: Silt loam, pH 6.4, OC 2.1% 19±1°C, 125-126 d	21.7/50.5 d (IORE)	CO_2: ≤ 8.1% AR NER: ≤ 43.9% AR	properties		
	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled 2 US soils: PCA: Sandy loam, pH 7.2, OC 0.69% LNE: Silt loam, pH 6.4, OC 2.1% 20±1°C, 120-125 d	**PCA:** DT_{50}/t_R = 92.9/92.9 d (SFO) **LNE:** DT_{50}/t_R = 35.3/78.8 d (DFOP)	**Major:** BCS-BP32808 **Minor:** BCS-CY96288 CO_2: ≤ 29.5% AR NER: ≤ 29.2% AR		Acceptable	3349343
	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled 4 German soils: HN: silt loam, pH 5.5, OC 2.8% AX: loamy sand, pH 5.9, OC 1.5% HH: silt loam, pH 6.2, OC 1.8% DD: clay loam, pH 7.0, OC 4.7%	**HN:** DT_{50}/t_R = 26.1/48.6 d (DFOP) **AX:** DT_{50}/t_R = 18.9/47.2 d (DFOP) **HH:** DT_{50}/t_R = 13.6/39.8 d	**Major:** BCS-DA63612, BCS-DC21250 **Minor:** BCS-CY96288 CO_2: ≤ 12.4% AR NER: ≤ 37.5% AR		Acceptable	3349342

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	20±2°C, 125 d	(DFOP) **DD:** DT_{50}/t_R = 19.8/41.3 d (DFOP)				
	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled 4 German soils: HN: silt loam, pH 5.5, OC 2.8% AX: loamy sand, pH 5.9, OC 1.5% HH: silt loam, pH 6.2, OC 1.8% DD: clay loam, pH 7.0, OC 4.7% 20±2°C, 125 d	**HN:** DT_{50}/t_R = 37.6/37.6 d (SFO) **AX:** DT_{50}/t_R = 16.3/42.7 d (DFOP) **HH:** DT_{50}/t_R = 12.7/42.8 d (DFOP) **DD:** DT_{50}/t_R = 19.2/46.8 d (IORE)	**Major:** BCS-CC26101 **Minor:** BCS-CY96288, BCS-CZ38260 CO_2: ≤ 33.9% AR NER: ≤ 31.9% AR		Acceptable	3349344
	Fluoxapiprolin [thiazolyl-2-^{14}C]-labelled AX: loamy sand, pH 6.2, OC 2.0%	**AX:** DT_{50}/t_R = 15.7/35.9 d (IORE)	**Major:** BCS-DA63612, BCS-DC21250 **Minor:** BCS-CY96288		Acceptable	3349345

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	20±2°C, 120 d		CO_2: ≤ 12.9% AR NER: ≤ 24.0% AR			
Biotransformation of transformation products in aerobic soil – TP used as the testing compound	BCS-BP32808 [pyrazole-4-^{14}C]-labelled 4 German soils: HN: silt loam, pH 5.2, OC 2.9% AX: sandy loam, pH 6.9, OC 1.7% HH: silt loam, pH 5.7, OC 2.3% DD: loam, pH 7.2, OC 5.4% 20±2°C, 28 d	**HN:** DT_{50}/t_R = 16.82/29.57 d (IORE) **AX:** DT_{50}/t_R = 3.38/4.65 d (IORE) **HH:** DT_{50}/t_R = 19.76/34.78 d (IORE) **DD:** DT_{50}/t_R = 8.01/17.81 d (IORE)	**Major:** BCS-CZ38260 **Minor:** None identified, max 14.0% AR CO_2: ≤ 49.7% AR NER: ≤ 37.6% AR	BCS-BP32808 (BCS-CS55621-BDM-pyrazole) is non-persistent to slightly persistent in aerobic soils. Note: the estimated DT_{50}/t_R from the study with the parent was 14.6 d (using parent-daughter fit)	Acceptable	3349350
	BCS-DG91934 (tested as BCS-DH17585, the Na^+ salt form, non-labelled)	**HN:** DT_{50}/t_R = 148.0/189.84 d (DFOP) **AX:**	**Major:** Not tracked **Minor:** Not tracked	BCS-DG91934 (BCS-CS55621-thiazole acid) is moderately persistent to persistent in aerobic	Acceptable	3349349

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	4 German soils: HN: silt loam, pH 5.3, OC 2.7% AX: sandy loam, pH 6.6, OC 1.7% HH: silt loam, pH 6.0, OC 1.8% DD: clay loam, pH 7.3, OC 4.7% 20±2°C, 120 d	DT_{50}/t_R = 135.6/190.62 d (DFOP) **HH:** DT_{50}/t_R = 214.1/321.24 d (DFOP) **DD:** DT_{50}/t_R = 129.9/129.9 d (SFO)	CO_2: Not tracked NER: Not tracked	soil.		
	BCS-DA63612 non-labelled 4 German soils: HN: silt loam, pH 5.3, OC 2.2% AX: loamy sand, pH 6.2, OC 1.4% HH: silt loam, pH 5.7, OC 1.7% DD: clay loam, pH 7.2, OC 4.8% 20±2°C, 120 d	**HN:** DT_{50}/t_R = 228.5/259.2 d (DFOP) **AX:** DT_{50}/t_R = 266.9/266.9 d (SFO) **HH:** DT_{50}/t_R = 272.3/303.1 d (DFOP) **DD:** DT_{50}/t_R = 315.1/357.4 d (DFOP)	**Major:** Not tracked **Minor:** Not tracked CO_2: Not tracked NER: Not tracked	BCS-DA63612 (BCS-CS55621-lactam) is persistent in aerobic soil.	Acceptable	3349351

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	BCS-DC21250 non-labelled 4 German soils: HN: loam, pH 5.4, OC 3.0% AX: sandy loam, pH 6.6, OC 1.5% HH: silt loam, pH 5.9, OC 2.1% DD: clay loam, pH 7.3, OC 5.3% 20±2°C, 122 d	**HN:** DT_{50}/t_R = 326.4/326.4 d (SFO) **AX:** DT_{50}/t_R = 128.2/261.1 d (DFOP) **HH:** DT_{50}/t_R = 388.7/388.7 d (SFO) **DD:** DT_{50}/t_R = 68.0/107.4 d (DFOP)	**Major:** Not tracked **Minor:** Not tracked CO_2: Not tracked NER: Not tracked	BCS-DC21250 (BCS-CS55621-piperidine) is classified as moderately persistent to persistent in aerobic soil	Acceptable	3349346
	BCS-CC26101 [acetic acid-2-^{14}C]-labelled 4 German soils: HN: loam, pH 5.5, OC 2.9% AX: loamy sand, pH 5.8, OC 1.8% HH: silt loam, pH 5.7, OC 2.2% DD: loam, pH 7.2, OC 5.2%	**HN:** DT_{50}/t_R = 0.91/1.91 d (SFO) **AX:** DT_{50}/t_R = 1.07/1.07 d (SFO) **HH:** DT_{50}/t_R = 0.99/0.99 d	**Major:** none **Minor:** One unidentified, max 2.4% AR CO_2: ≤ 53.9% AR NER: ≤ 47% AR	BCS-CC26101 (BCS-CS55621-pyrazole-acetic acid) in non-persistent in aerobic soil	Acceptable	3349347

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	20±2°C, 4 d	(SFO) **DD:** DT_{50}/t_R = 0.70/0.70 d (SFO)				
	BCS-CZ38260 [pyrazole-4-^{14}C]-labelled 4 German soils: HN: loam, pH 5.5, OC 3.9% AX: loamy sand, pH 5.8, OC 1.7% HH: silt loam, pH 6.0, OC 2.3% DD: loam, pH 7.2, OC 5.2% 20±2°C, 30 to 57 d	**HN:** DT_{50}/t_R = 4.95/4.95 d (SFO) **AX:** DT_{50}/t_R = 5.91/5.91d (SFO) **HH:** DT_{50}/t_R = 10.40/10.40 d (SFO) **DD:** DT_{50}/t_R = 10.37/10.37 d (SFO)	**Major:** none **Minor:** Sum of unidentified (4) and unresolved, max at 16.3% AR CO_2: ≤ 50.6% AR NER: ≤ 44.0% AR	BCS-CZ38260 (BCS-CS55621-pyrazole carboxylic acid) is non-persistent in aerobic soil	Acceptable	3349348
Biotransformation in anaerobic soil	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled German soil: AX: sandy loam,	**Anaerobic:** DT_{50}/t_R = 260/260 d (SFO)	**Major:** none after flooding **Minor:** BCS-CS55621-4-OH-piperidine and	Fluoxapiprolin is persistent in anaerobic soils. Biotransformation in anaerobic soil is	Acceptable with limitations (anaerobic conditions were not	3349353

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	pH 5.3, OC 1.2% 20±2°C, 14 d aerobic incubation and 120 d anaerobic (flooded) incubation		more than 9 minor unknowns CO_2 none after flooding NER ≤ 24.5% AR	not an important route of dissipation for fluoxapiprolin.	fully established until mid-way of the study in both cases)	
	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled German soil: AX: sandy loam, pH 5.3, OC 1.2% 20±2°C, 14 d aerobic incubation and 120 d anaerobic (flooded) incubation	**Anaerobic:** DT_{50}/t_R = 367/367 d (SFO)	**Major:** none after flooding **Minor:** BCS-CS55621-4-OH-piperidine, BCS-CS55621-pyrazole-carboxylic acid and potentially BCS-CS55621-pyrazole acetic acid (primarily formed prior to flooding); more than 15 minor unknowns CO_2 none after flooding NER ≤ 23.1% AR			3349354

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
Biotransformation in aerobic water/sediment systems	Fluoxapiprolin [phenyl-UL-^{14}C]-labelled ANG, Germany: water: pH 7.8, <2 ppm DOC; sediment: sand, pH 6.6, 0.76% OC WIE, Germany: water: pH 7.6, 3 ppm DOC; sediment: sandy loam, pH 5.1, 6.5% OC 20±2°C, 100 d	ANG: Water DT_{50}/t_R = 0.83/8.08 d (DFOP) Total system DT_{50}/t_R = 21.8/21.8 d (SFO) WIE: Water DT_{50}/t_R = 0.70/2.47 d (IORE) Total system DT_{50}/t_R = 36.48/63.06 d (IORE)	**Major:** BCS-CS55621-lactam (BCS-DA63612) **Minor:** BCS-CS55621-4-OH-piperidine (BCS-CY96288) CO_2 ≤ 2.7% AR NER < 38.9% AR	Fluoxapiprolin is slightly persistent in aerobic aquatic systems. Biotransformation in aerobic water/sediment systems is an important route of dissipation for fluoxapiprolin.	Acceptable	3349355
	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled ANG, Germany: water: pH 7.8, 3 ppm DOC; sediment: sand, pH 6.6, 0.76% OC WIE, Germany: water: pH 7.6, 4 ppm DOC; sediment: sand, pH	ANG: Water DT_{50}/t_R = 0.89/2.33 d (IORE) Total system DT_{50}/t_R = 17.66/17.66 d (SFO) WIE: Water DT_{50}/t_R = 0.50/2.96 d (IORE) Total system	**Major:** BCS-CC26101, BCS-CZ38260 and BCS-CY96288 **Minor:** more than 11 unidentified CO_2: 37.5% AR in ANG and 1.2% AR in WTE		Acceptable	3349356

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	5.1, 6.5% OC 20±2°C, 100 d	DT_{50}/t_R = 38.85/38.85 d (SFO)	NER ≤ 28.6% AR			
Biotransformation in anaerobic water/sediment systems	Fluoxapiprolin [Phenyl-UL-^{14}C]-labelled GR, USA: water pH 8.2, 7.7 ppm DOC; sediment texture: silt loam, pH 7.7, 3.8% OC [pyrazole-4-^{14}C]-labelled GL, USA: water pH 8.3, 11.8 ppm DOC; sediment texture: loamy sand, pH 8.0, 1.0% OC 20±2°C, 105 d	GR: Water DT_{50}/t_R = 3.06/3.06 d (SFO) Total system DT_{50}/t_R = 133.7/258.5 d (DFOP) GL: Water DT_{50}/t_R = 2.50/4.16 d (IORE) Total system DT_{50}/t_R = 110.2/110.2 d (SFO)	**Major:** BCS-DM16188 (BCS-CS55621-dihydroxy) and BCS-DG54513 (BCS-CS55621-keto-hydroxy) **Minor:** up to 6 unidentified CO_2 ≤ 0.1% AR NER ≤ 23.8% AR	Fluoxapiprolin is moderately persistent in anaerobic aquatic systems. Biotransformation in anaerobic water/ sediment systems may contribute to the overall dissipation of fluoxapiprolin.	Acceptable	3349358
Mobility						
Adsorption / desorption of the parent compound	Fluoxapiprolin [pyrazole-4-^{14}C]-labelled Two US soils and	K_d: 92.7–329.8 mL/g K_{oc}: 13 239–19 400 mL/g OC	N/A	Fluoxapiprolin is classified as immobile in soil	Acceptable with limitations (complete dissolution	3349362

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	one Japanese Volcanic soil (results not included here)				of the highest concentration was not achieved and result was excluded in calculating K_d/K_{oc}; soil: solution ratio was not appropriate)	
	Fluoxapiprolin [Phenyl-UL-^{14}C]-labelled Three German soils	K_d: 239–592 mL/g K_{oc}: 9565–13264 mL/g OC	N/A		Acceptable with limitations (time for equilibrium was not fully established)	3480767
Adsorption / desorption of the transformation products	BCS-CS55621-BDM-pyrazole (BCS-BP32808) [Pyrazole-4-^{14}C]-labelled Five German soils	K_d: 0.08–0.39 mL/g K_{oc}: 7.54–12.68 mL/g OC	N/A	BCS-CS55621-BDM-pyrazole is classified as having very high mobility	Acceptable	3349372
	BCS CS55621-thiazole acid (BCS-DG91934, tested with BCS-DH34157-NH_4^+ salt)	K_d: 5.30–13.26 mL/g K_{oc}: 217–283 mL/g OC	N/A	BCS CS55621-thiazole acid is classified as having medium mobility	Acceptable	3349375

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	[Phenyl-UL-^{14}C]-labelled Four German soils					
	BCS-CS55621-lactam (BCS-DA63612) [Phenyl-UL-^{14}C]-labelled Four German soils	K_d: 32.3–85.7 mL/g K_{oc}: 1647–2264 mL/g OC	N/A	BCS-CS55621-lactam is classified as having low to slight mobility	Acceptable	3349370
	BCS-CS55621-piperidine (BCS-DC21250, tested with BCS-CU97237-HCl salt) [Phenyl-UL-^{14}C]-labelled Four German soils	K_d: 99.6–299 mL/g K_{oc}: 5307–8647 mL/g OC	N/A	BCS-CS55621-piperidine is classified as immobile	Acceptable	3349366
	BCS-CS55621-pyrazole acetic acid (BCS-CC26101) [Acetic acid-2-^{14}C]-labelled Four German soils	K_d: 0.022–0.084 mL/g K_{oc}: No correlation with %OC	N/A	BCS-CS55621-pyrazole acetic acid is classified as having very high mobility	Acceptable with limitations (analytically unreliable due to minimum adsorption)	3349368
	BCS-CS55621-4-OH-piperidine (BCS-CY96288)	K_d: 33.5–198.5 mL/g	N/A	BCS-CS55621-4-OH-piperidine is classified as having	Acceptable	3349364

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	[Acetyl-2-^{14}C]-labelled Two US soils and three German soils	K_{oc}: 3758–8229 mL/g OC		slight mobility to immobile		
Volatilization	Fluoxapiprolin is not expected to be volatile under field conditions. Although the calculated Henry's law constant suggests that there is a low potential for volatilization, there were limited detection of volatile organics in volatile traps in the laboratory studies. Transformation products of fluoxapiprolin are not expected to be volatile under field conditions based on calculated or estimated Henry's law constants and supported by low detection of volatile organics in volatile traps in the laboratory studies.					N/A
Field studies						
Terrestrial field dissipation	BCS-CS55621 SC20 formulation (1.93% w/w, 20 g a.i./L) Bare ground, Ontario, Canada Loam; % OC 2.7; pH 7.3 (0-15 cm layer) Single application rate: 60 g a.i./ha Study duration: 390 days	Bare ground: DT_{50}/t_R = 61.0 days (SFO) Residues found were mostly confined to the uppermost soil layers of 0–15 cm, between LOD and LOQ in 15–30 cm and trace amounts below the 30-cm depth. 330–390 days	Seven TPs were monitored: BCS-CY96288 was a major TP, formed at a maximum of 6.4 g peq/ha (10.7% of parent) after 62 days of application. BCS-BP32808: 1.9% BCS-CU97237: 2.2% BCS-DA63612: 1.1% BCS-CZ38260:	Overall, fluoxapiprolin and its soil transformation products have low leaching potential and are not expected to accumulate in soil.	Acceptable with limitations due to insufficient moisture input during the initial 4 months, affecting leaching assessment	3349572

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
		after application, 11.4–5.36% of the target amount remained	2.0% BCS-DH17585: 1.2% BCS-CC26101: 0.9%			
	BCS-CS55621 SC20 formulation (1.94% w/w, 20 g a.i./L) Bare ground, Iowa, USA Silty clay loam; % OC 2.0; pH 7.5 (0-15 cm layer) Single application rate: 60 g a.i./ha Study duration: 511 days	Bare ground: DT_{50}/t_R = 80.4 days (SFO) Residues found were mostly confined to the uppermost soil layers of 0–15 cm, and trace amounts below the 15–cm depth. After about a year (351 days), 8.0% of the target amount remained	Seven TPs were monitored: BCS-CY96288 was a major TP, formed at a maximum of 7.0 g peq/ha (11.7% of parent) after 113 days of application. BCS-BP32808: 2.4% BCS-CU97237: 1.5% BCS-DA63612: 0.7% BCS-CZ38260: <LOD BCS-DH17585: <LOD BCS-CC26101: 1.4%		Acceptable	3349573
	BCS-CS55621 SC20 formulation	Bare ground: DT_{50}/t_R =	Seven TPs were monitored:		Acceptable	3349577

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	(1.93% w/w, 20 g a.i./L) Bare ground, Washington, USA Sand; % OC 0.21; pH 8.4 (0–15 cm layer) Single application rate: 60 g a.i./ha Study duration: 365 days	19.7/43.9 days (IORE) Residues found were mostly confined to the uppermost soil layers of 0–15 cm, with one detect at near LOD and rest either at trace level or non-detect at 15–30 cm depth, and non-detect in depth below 30 cm. After one year of application, only trace amount (< LOD) remained	BCS-CY96288 formed the most at a maximum of 5.5 g peq/ha (9.2% of parent) after 181 days of application. BCS-BP32808: 0.8% BCS-CU97237: 0.3% BCS-DA63612: 0.6% BCS-CZ38260: 3.6% BCS-DH17585: 1.0% BCS-CC26101: 0.5% BCS-CZ38260 was observed between LOD and LOQ three times, one of which was at 30-45 cm depth.			

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	BCS-CS55621 SC20 formulation (1.93% w/w, 20 g a.i./L) Bare ground, CA, USA (irrelevant to Canada) Loamy sand; % OC 0.29; pH 7.5 (0–15 cm layer) Single application rate: 60 g a.i./ha Study duration: 358 days	Bare ground: DT_{50}/t_R = 37.3 days (SFO) Residues found were mostly confined to the uppermost soil layers of 0-15 cm, with one detect at near LOD, one detect near LOQ and the rest either at trace level or non-detect at 15-30 cm depth, and non-detect in depth below 30 cm. After one year of application, only trace amount (< LOD) remained	Seven TPs were monitored: BCS-CY96288 formed as a major TP at a maximum of 6.5 g peq/ha (10.9% of parent) after 14 days of application. BCS-BP32808: none BCS-CU97237: 0.7% BCS-DA63612: 0.7% BCS-CZ38260: 2.3% BCS-DH17585: 3.6% BCS-CC26101: 0.3%		Acceptable as supporting information since test site is irrelevant to Canada	3349575

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
	BCS-CS55621 SC20 formulation (1.93% w/w, 20 g a.i./L) Bare ground, Georgia, USA (irrelevant to Canada) Loamy sand; % OC 0.42; pH 6.7 (0–15 cm layer) Single application rate: 60 g a.i./ha Study duration: 341 days	Bare ground: DT_{50}/t_R = 34.0 days (SFO) Residues found were mostly confined to the uppermost soil layers of 0-15 cm, with two detect above LOD, one detect near LOQ and the rest either at trace level or non-detect at 15-30 cm depth, and non-detect in depth below 30 cm. After one year of application, 4.24% remained	Seven TPs were monitored and all were detected in 0-15 cm layer and trace amounts below (except a few near LOD). Maximum were: BCS-CY96288: 7.1% BCS-BP32808: 6.1% BCS-CU97237: 2.6% BCS-DA63612: 2.6% BCS-CZ38260: 2.4% BCS-DH17585: 1.5% BCS-CC26101: 0.6%		Acceptable as supporting information since test site is irrelevant to Canada	3349576
Aquatic field dissipation	No aquatic field dissipation study with fluoxapiprolin was submitted and none is required.					

Study type	Test material/test system	Value[1]	Transformation products	Comments	Study acceptability	References (PMRA No.)
Bioconcentration/bioaccumulation						
Bioconcentration in fish	Fluoxapiprolin Flow-through bioconcentration study Bluegill sunfish (*Lepomis macrochirus*) were exposed to [pyrazole-4-^{14}C] fluoxapiprolin at nominal concentrations of 0.5 µg/L and 5 µg/L for an uptake period of 28 days, followed by a depuration period of 14 days.	BCF_K TRR = 11.0 and 11.7 L/kg for whole fish; BCF_K TRR = 23.6 and 24.9 L/kg for non-edible (low dose and high dose, respectively) BCF_{SS} TRR = 8.93 and 9.61 L/kg for whole fish; BCF_{SS} TRR = 19.1 and 20.3 L/kg for non-edible (low dose and high dose, respectively)	In edible (max % TRR): 3-OH-propyl (14.4%) Unknown 6 (14.3%) In non-edible (max % TRR): 4-OH piperidine (29.2%) 3-OH-propyl-4-OH (12.8%) 3-OH-propyl (9.0%)	Fluoxapiprolin does not readily bioconcentrate in fish tissue under the conditions of the study.	Acceptable	3349482

Table 17 Estimated environmental concentrations/exposures for screening level assessment

Environmental exposure matrix	Application	Conversion considerations	Estimated environmental exposure (EEC[1]/ED[2]/ EDE[3])	Notes
Soil	3 × 20 g a.i./ha 7-day interval	Aerobic soil half-life: 59.8 days (90% of upper confidence bound on the mean)	Soil surface EEC: 55.4 g a.i./ha	Used for terrestrial plant seedling emergence risk assessment
			Soil EEC: 0.025 mg a.i./kg soil (assuming homogeneous mixing in 0-15 cm depth with a soil bulk density of 1.5 g/cm^3)	Used for soil invertebrates risk assessment
	BCS-CS 55621-BDM-pyrazole 15.5 g peq/ha	100% conversion from annual application rate (60 g/ha × 168.1/650.1)	Soil EEC: 0.007 mg/kg soil (assuming homogeneous mixing in 0-15 cm depth with a soil bulk density of 1.5 g/cm^3)	Used for soil invertebrates risk assessment
Plant	3 × 20 g a.i./ha 7-day interval	Foliar half-life: 10 days	EEC: 39.9 g a.i./ha	Used for the terrestrial plant vegetative vigour and foliar dwelling beneficial arthropods risk assessment
Spray droplets on surface of bees	1 × 20 g a.i./ha	2.4 µg a.i./bee/day per kg a.i./ha	ED: 0.048 µg a.i./bee	Used for assessing adult bees contact exposure
Food source: pollen and nectar	1 × 20 g a.i./ha	28.62 µg a.i./bee/day per kg a.i./ha	ED: 0.572 µg a.i./bee/day	Used for assessing adult bees oral exposure
Food source: pollen and nectar	1 × 20 g a.i./ha	12.15 µg a.i./bee/day per kg a.i./ha	ED: 0.243 µg a.i./bee/day	Used for assessing larvae oral exposure
Food source: insects	3 × 20 g a.i./ha 7-day interval	Foliar half-life: 10 days, FIR = 5.1 g dw diet/day	EDE: 3.25 mg a.i./kg bw/day	Used for small insectivorous bird (bw 20 g) risk assessment
Food source: insects	3 × 20 g a.i./ha 7-day interval	Foliar half-life: 10 days, FIR = 19.9 g dw diet/day	EDE: 2.54 mg a.i./kg bw/day	Used for medium insectivorous bird (bw 100 g) risk assessment
Food source:	3 × 20 g	Foliar half-life: 10 days,	EDE: 1.64 mg a.i./kg bw/day	Used for large herbivorous bird (bw

Environmental exposure matrix	Application	Conversion considerations	Estimated environmental exposure (EEC[1]/ED[2]/ EDE[3])	Notes
short grass	a.i./ha 7-day interval	FIR = 58.1 g dw diet/day		1000 g) risk assessment
Food source: insects	3 × 20 g a.i./ha 7-day interval	Foliar half-life: 10 days, FIR = 2.2 g dw diet/day	EDE: 1.85 mg a.i./kg bw/day	Used for small insectivorous mammal (bw 15 g) risk assessment
Food source: short grass	3 × 20 g a.i./ha 7-day interval	Foliar half-life: 10 days, FIR = 4.4 g dw diet/day	EDE: 3.52 mg a.i./kg bw/day	Used for medium herbivorous mammal (bw 35 g) risk assessment
Food source: short grass	3 × 20 g a.i./ha 7-day interval	Foliar half-life: 10 days, FIR = 68.7 g dw diet/day	EDE: 1.94 mg a.i./kg bw/day	Used for large herbivorous mammal (bw 1000 g) risk assessment
Food source: insects	BCS-CS 55621-BDM-pyrazole 15.5 g/ha	FIR = 2.2 g dw diet/day	EDE: 0.72 mg/kg bw/day	Used for small insectivorous mammal (bw 15 g) risk assessment
Food source: short grass	BCS-CS 55621-BDM-pyrazole 15.5 g TP/ha	FIR = 4.4 g dw diet/day	EDE: 1.37 mg./kg bw/day	Used for medium herbivorous mammal (bw 35 g) risk assessment
Food source: short grass	BCS-CS 55621-BDM-pyrazole 15.5 g TP/ha	FIR = 68.7 g dw diet/day	EDE: 0.75 mg/kg bw/day	Used for large herbivorous mammal (bw 1000 g) risk assessment
Fresh water	3 × 20 g a.i./ha 7-day interval	Aerobic water/sediment whole system half-life: 45.6 days (80th percentile), assuming instantaneous and homogeneous mixing in the specified depth	EEC (0-15 cm depth): 0.036 mg a.i./L	Used for amphibian risk assessment
			EEC (0-80 cm depth): 0.0068 mg a.i./L	Used for all aquatic organism risk assessment

Environmental exposure matrix	Application	Conversion considerations	Estimated environmental exposure (EEC[1]/ED[2]/ EDE[3])	Notes
	BCS-CS 55621-lactam 42.1 g TP/ha	100% conversion from annual application rate (60 g/ha × 455.9/650.1)	EEC (0-80 cm depth): 0.005 mg a.i./L	Used for pelagic arthropods risk assessment
Estuary/marine water	3 × 20 g a.i./ha 7-day interval	Aerobic water/sediment whole system half-life: 45.6 days (80th percentile), assuming instantaneous and homogeneous mixing in 0-80 cm depth	EEC (0-80 cm depth): 0.0068 mg a.i./L	Used for estuary/marine organism screening level risk assessment

[1] EEC = Estimated environmental concentration (mg a.i./kg or mg a.i./L) in soil or water

[2] ED = Estimated dose (µg a.i./bee) for bees, calculated by converting the maximum single application rate (20 g a.i./ha) by the conversion factor listed in the table. Adult conversion 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 conversion 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).

[3] EDE = Estimated Daily Exposure (mg a.i./kg bw/day) for birds and mammals, specialized feeding guilds are considered for each category of animal weight to help determine exposure (herbivore, frugivore, insectivore and granivore). At the screening level, relevant food items representing the most conservative EDE for each feeding guild are used (in other words, insects and short grasses). The EDE is calculated using the following formula: (FIR/bw) × EEC, where: bw = body weight, FIR = Food ingestion rate: 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: FIR (g dry weight/day) = 0.398 (bw in g)$^{0.850}$. All birds Equation: 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)$^{0.822}$

TPs**:** Application rates of the TPs were estimated by assuming 100% conversion from annual application rate of the parent with adjustment of the molecular weights; for BCS-CS55621-BDM-pyrazole: 168.1/650.1, and for BCS-CS 55621-lactam: 455.9/650.1.

Table 18 Effects of fluoxapiprolin, its formulation and transformation products on terrestrial organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Invertebrates						
Earthworm, *Eisenia andrei*	14-d Acute Artificial soil	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	Mortality: 14-d LC_{50} > 945 mg a.i./kg soil dw Sub-lethal effects (changes in body weight): 14-d EC_{50} > 945 mg a.i./kg soil dw No effects were observed up to the highest test concentration.	N/A	Acceptable	3349395
Earthworm, *Eisenia fetida*	14-d Acute Artificial soil	BCS-CS55621 20 SC End-use product, containing 20.13 g a.i./L (1.92% w/w)	Mortality: **14-d LC_{50} > 1000 mg end-use product/kg soil dw (>19.2 mg a.i./kg soil dw)** Sub-lethal effects (changes in body weight): 14-d EC_{50} > 1000 mg end-use product/kg soil dw (>19.2 mg a.i./kg soil dw)	N/A	Acceptable	3349653
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621 20 SC End-use product, containing 20.13 g a.i./L (1.92% w/w)	28-d adult mortality: LC_{50} > 1000 mg end-use product/kg soil dw (19.2 mg a.i./kg soil dw) NOEC ≥ 1000 mg end-ise product/kg soil dw (19.2 mg a.i./kg soil dw) Reproduction: **NOEC ≥ 1000 mg end-use**	N/A	Acceptable	3349654

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
			product/kg soil dw (19.2 mg a.i./kg soil dw)			
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-BDM-pyrazole (BCS-BP32808) (TP, purity: 99.9%)	28-d adult mortality: LC_{50} > 100 mg/kg soil dw NOEC ≥ 100 mg/kg soil dw Reproduction: EC_{50} > 100 mg/kg soil dw NOEC = 32 mg/kg soil dw Significant reduction of number of juveniles at the two highest test concentrations	N/A	Acceptable	3349388
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-pyrazole acetic acid (BCS-CC26101) TP, purity: 99.6%	28-d adult mortality: LC_{50} > 100 mg/kg soil dw NOEC ≥ 100 mg/kg soil dw Reproduction: NOEC ≥ 100 mg/kg soil dw No effects on mortality/growth/ reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349389
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-thiazole acid (sodium salt) (BCS-DH17585) TP, purity: 92.4%	28-d adult mortality: LC_{50} > 100 mg/kg soil dw NOEC ≥ 100 mg/kg soil dw Reproduction: NOEC ≥ 100 mg/kg soil dw No effects on mortality/growth/ reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349390

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-lactam (BCS-DA63612) TP, purity: 98.6%	28-d adult mortality: LC_{50} > 1000 mg/kg soil dw NOEC ≥ 1000 mg/kg soil dw Reproduction: NOEC ≥ 1000 mg/kg soil dw No effects on mortality/growth/ reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349391
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-4-OH piperidine (BCS-CY96288) TP, purity: 96.8%	28-d adult mortality: LC_{50} > 100 mg/kg soil dw NOEC ≥ 100 mg/kg soil dw Reproduction: NOEC ≥ 100 mg/kg soil dw No statistically significant effects on mortality/growth/ reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349392

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-4- piperidine (HCl salt) (BCS-CU97237) TP, purity: 97.2%	28-d adult mortality: LC_{50} > 100 mg/kg soil dw NOEC ≥ 100 mg/kg soil dw Reproduction: NOEC ≥ 100 mg/kg soil dw No statistically significant effects on mortality/growth/ reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349393
Earthworm, *Eisenia fetida*	56-d chronic Artificial soil	BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260) TP, purity: 98.3%	28-d adult mortality: LC_{50} > 100 mg/kg soil dw NOEC ≥ 100 mg/kg soil dw Reproduction: NOEC ≥ 100 mg/kg soil dw No statistically significant effects on mortality/growth/ reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349394
Honey bee, *Apis mellifera*	48-h Oral and contact limit test, adults	(Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	Acute oral LD_{50}: > 217.6 µg a.i./bee Acute Contact LD_{50}: > 200 µg a.i./bee No toxic effects at the test doses.	Practically non-toxic	Acceptable	3349396

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Honey bee, *Apis mellifera*	96-h acute oral (full test) and 48-h acute contact (limit test), adults	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92% w/w)	96-h oral LD_{50}: **42.3 µg a.i./bee** 95% C.I.: 29.2–51.4 µg a.i./bee (mortality was 50-100%, and LD_{50} was extrapolated below the range of actual intake doses) **48-h contact LD_{50}: > 100 µg a.i./bee** No toxic effects at the test doses.	Practically non-toxic	Acceptable for acute contact portion and acceptable with limitations for the acute oral portion.	3349655
Honey bee, *Apis mellifera*	48-h Acute oral/contact limit test, adult	BCS-CS55621-pyrazole-acetic acid (a metabolite of fluoxapiprolin), purity: 99.6%	Acute oral LD_{50}: > 106.6 µg/bee Acute Contact LD_{50}: > 100 µg/bee No toxic effects at the test doses.	Practically non-toxic	Acceptable	3349397
Honey bee, *Apis mellifera*	48-h Acute oral/contact limit test, adult	BCS-CS55621-pyrazole-methylsulfinyl acid (BCS-DE72760) (a metabolite of fluoxapiprolin), purity: 94.6%	Acute oral LD_{50}: > 107.6 µg/bee **Acute Contact LD_{50}: > 50 µg/bee** No toxic effects at the test doses. It is noted that this chemical was not identified in any of the fate studies.	Practically non-toxic	Acceptable	3349401

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Honey bee, *Apis mellifera*	48-h Acute oral/contact limit test, adult	BCS-CS55621-pyrazole-alanine-oxopropanoic acid (BCS-DE72761) (a metabolite of fluoxapiprolin), purity: 97.9%	Acute oral LD_{50}: > 110.2 µg/bee Acute Contact LD_{50}: > 100 µg/bee No toxic effects at the test doses. It is noted that this chemical was not identified in any of the fate studies.	Practically non-toxic	Acceptable	3349403
Honey bee, *Apis mellifera*	48-h Acute oral/contact limit test, adult	BCS-CS55621-pyrazole-alanine (BCS-DE61185) (a metabolite of fluoxapiprolin), purity: 96.2%	Acute oral LD_{50}: > 110.1 µg/bee Acute Contact LD_{50}: > 50 µg/bee No toxic effects at the test doses. It is noted that this chemical was not identified in any of the fate studies.	Practically non-toxic	Acceptable	3349339
Honey bee, *Apis mellifera*	10-d Chronic feeding, adults	Fluoxapiprolin, Technical grade active ingredient, purity: 94.5%	LD_{50} > 39 µg a.i./bee/day NOAED = 39 µg a.i./bee/day No dose-responsive mortality or sublethal effects were observed up to the highest dose level.	N/A	Acceptable	3349410
Honey bee, *Apis mellifera*	10-d Chronic (repeated exposure), adult	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92%	10-d-LD_{50}: 20 µg a.i./bee/day **10-d-NOAED = 12 µg a.i./bee/day** 10-d-LOAED = 22 µg a.i./bee/day	N/A	Acceptable	3349662

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
		w/w)	Bee mortality was the most sensitive endpoint.			
Honey bee, *Apis mellifera*	8-d Chronic larva (repeated exposure), limit test	Fluoxapiprolin Technical grade active ingredient, purity: 98.5%	8-d-LD_{50} > 25.3 µg a.i./larva/day 8-d-NOAED = 25.3 µg a.i./larva/day No larval mortality or sublethal effects at the limit test dose.	N/A	Acceptable with limitations (not a full length guideline study)	3349407
Honey bee, *Apis mellifera*	22-d Chronic, larva	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	**8-d-LD_{50} > 18.5 µg a.i./larva/day** 22-d-NOAED = 18.5 µg a.i./larva/day No dose-responsive effects on larval mortality (8-d) and adult emergence (22-d) up to the highest measured dose.	N/A	acceptable	3349408
Honey bee, *Apis mellifera*	22-d Chronic, larva	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92% w/w)	8-d-LD_{50} > 21.0 µg a.i./larva/day **22-d-NOAED = 4.8 µg a.i./larva/day** (emergence) All endpoints were significantly affected in the two highest test levels, and adult emergence was the most sensitive endpoint.	N/A	acceptable	3349660

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Honey bee (*Apis mellifera*) hive in tunnels (semi-field test); Germany	Test item was applied to flowering lacy phacelia (*Phacelia tanacetifolia*) at 20 g a.i./ha, applied twice one day apart; one before bee flight and one during bee flight. Duration: 7-d exposure; 43-d including post application monitoring.	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L	**Effects:** No significant biologically relevant effects on any measurement endpoint evaluated (mortality, flight intensity, behaviour, and colony condition and strength) from foliar application of fluoxapiprolin as BCS-CS55621 SC 20. **Residues:** Bee-collected pollen represented the matrix with the highest residues of fluoxapiprolin (2.2 mg a.i./kg). Nectar residues were 0.056 mg a.i./kg. Residues declined by 88% on DAA1.	N/A	Acceptable	3349664
Honey bee (*Apis mellifera*) hive in tunnels (semi-field test); Spain			**Effects:** No significant or biologically relevant effects on any measurement endpoint evaluated (mortality, flight intensity, behaviour, and colony condition and strength) from foliar application of fluoxapiprolin as BCS-CS55621 SC 20. **Residues:** The highest residues were detected in pollen from foraging bees, at 4.110 mg a.i./kg. Residues in nectar were 0.0910 mg a.i./kg. Residues declined by 83% by DAA1.	N/A	Acceptable	3349666

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Bumble bee (*Bombus terrestris*)	48-h Oral, limit test, adults	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	LD_{50} > 231.6 µg a.i./bee No mortality and sublethal effects were observed.	Practically non-toxic (based on honeybee classification scheme)	Acceptable	3349405
	48-h Contact, limit test, adults		LD_{50} > 200 µg a.i./bee No mortality and sublethal effects were observed.	Practically non-toxic (based on honeybee classification scheme)		
Bumble bee (*Bombus terrestris*)	48-h Oral, adults	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92% w/w)	**LD_{50} > 117 µg a.i./bee** No treatment related mortality or behavioural effects were observed up to the highest test concentration. (Non-feeders were excluded from endpoint determination.)	Practically non-toxic (based on honeybee classification scheme)	Acceptable	3349657
	48-h Contact, adults		**LD_{50} > 100 µg a.i./bee** No treatment related mortality or behavioural effects were observed up to the highest test concentration.	Practically non-toxic (based on honeybee classification scheme)		
Predatory mite, *Typhlodromus pyri*	14-d Contact, glass plates	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92% w/w)	7-d mortality: **LR_{50}: > 60 g a.i./ha** Reproduction: ER_{50}: > 60 g a.i./ha **NOAER ≥ 60 g a.i./ha**	N/A	Acceptable	3349667
Parasitoid wasp, *Aphidius rhopalosiphi*	14-d Contact, glass plates	BCS-CS55621 SC 20 End-use product, containing	48-hr mortality: **LR_{50}: > 60 g a.i./ha** Reproduction:	N/A	Acceptable	3349668

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
		20.13 g a.i./L (1.92% w/w)	**NOAER ≥ 60 g a.i/ha** There were no statistically significant effects on survival or reproduction at any of the treatment levels tested.			
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92% w/w)	NOAEC ≥ 1000 mg End-use product/kg dw soil (NOAEC ≥ 19.2 mg a.i./kg dw soil) LOAEC > 1000 mg End-use product/kg dw soil (LOAEC > 19.2 mg a.i./kg dw soil) LC_{50}/EC_{50} > 1000 mg End-use product/kg dw soil (LC_{50}/EC_{50} > 19.2 mg a.i./kg dw soil) No treatment-related effects on mortality or reproduction were observed at the highest test concentration.	N/A	Acceptable	3349670
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621-pyrazole-acetic acid (BCS-CC26101), TP, purity: 99.6%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed at the highest test concentration.	N/A	Acceptable	3349414
Killer mite, *Hypoaspis*	14-d Contact, artificial soil	BCS-CS55621-thiazole acid	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil	N/A	Acceptable	3349415

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
aculeifer		(sodium salt, BCS-DH17585) TP, purity: 92.4%	No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.			
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621-lactam (BCS-DA63612) TP, purity: 98.6%	NOAEC ≥ 1000 mg/kg dw soil LOAEC > 1000 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed at the highest test concentration.	N/A	Acceptable	3349416
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260) TP, purity: 98.3%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349413
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621-piperidine (HCl salt) (BCS-CU97237) TP, purity: 97.2%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349412
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621-BDM-pyrazole (BCS-BP32808) TP, purity:	Mortality: NOAEC = 32 mg/kg dw soil LOAEC = 56 mg/kg dw soil Reproduction:	N/A	Acceptable	3349411

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
		99.9%	EC_{10} = 33 (95% C.I.: 28-37 mg/kg dw soil) NOAEC = 18 mg/kg dw soil Increased mortality and reduced reproduction			
Killer mite, *Hypoaspis aculeifer*	14-d Contact, artificial soil	BCS-CS55621-4-OH piperidine (BCS-CY96288) TP, purity: 96.8%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349417
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621 SC 20 End-use product, containing 20.13 g a.i./L (1.92% w/w)	**NOAEC ≥ 1000 mg End-use product/kg dw soil (NOAEC ≥ 19.2 mg a.i./kg dw soil)** LOAEC > 1000 mg End-use product/kg dw soil (LOAEC > 19.2 mg a.i./kg dw soil) No treatment-related effects on mortality or reproduction were observed at the highest test concentration.	N/A	Acceptable	3349669
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-pyrazole-acetic acid (BCS-CC26101) TP, purity: 99.6%	NOAEC ≥ 100 mg/kg dw soil LOAEC >100 mg/kg dw soil No treatment-related effects on mortality or reproduction	N/A	Acceptable	3349442

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
			were observed at the highest test concentration.			
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-thiazole acid (sodium salt, BCS-DH17585) TP, purity: 92.4%	NOAEC: 56 mg/kg dw soil LOAEC: 100 mg/kg dw soil Reproduction was affected at the highest test concentration (10% reduction).	N/A	Acceptable	3349443
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-lactam (BCS-DA63612) TP, purity: 98.6%	NOAEC ≥ 1000 mg/kg dw soil LOAEC > 1000 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed at the highest test concentration.	N/A	Acceptable	3349445
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260) TP, purity: 98.3%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349441
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-piperidine (HCl salt) (BCS-CU97237) TP, purity: 97.2%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349439

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-BDM-pyrazole (BCS-BP32808) TP, purity: > 99.9%	Mortality: NOAEC = 9 mg/kg dw soil LC_{10} = 8.4 (6.9-10.3) mg/kg dw soil (combining two sets of tests) Reproduction: NOAEC = 9 mg/kg dw soil **EC_{10} = 8.1 (7.5-8.6) mg/kg dw soil** (combining two sets of tests) Increased mortality and reduced reproduction.	N/A	Acceptable	3349438
Collembolan, *Folsomia candida*	28-d Contact, artificial soil	BCS-CS55621-4-OH piperidine (BCS-CY96288) TP, purity: 96.8%	NOAEC ≥ 100 mg/kg dw soil LOAEC > 100 mg/kg dw soil No treatment-related effects on mortality or reproduction were observed up to the highest test concentration.	N/A	Acceptable	3349444
Birds						
Bobwhite quail, *Colinus virginianus*	Acute Oral, limit test	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	LD_{50} > 2000 mg a.i./kg bw No mortality occurred; reduction in food consumption was observed during the first three days and was recovered thereafter.	Practically non-toxic	Acceptable	3349483
	Acute Oral, limit test	BCS-CS55621 SC 20 End-use product, containing	**LD_{50} > 2000 mg End-use product/kg bw** **(LD_{50} > 38.8 mg a.i./kg bw)**	Practically non-toxic for End-use product	Acceptable	3349673

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
		1.94% w/w fluoxapiprolin	No mortality occurred. Side effects included lack of feces, very little feces, and/or diarrhea on the day of dosing, but resolved by the end of the day.			
	5-d Dietary	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	LC_{50} > 4646 mg a.i./kg diet **LD_{50} > 964 mg a.i./kg bw/day** No mortality or dose-responsive sublethal effects observed up to the highest dose level.	Non-toxic up to the highest dose level	Acceptable	3349485
	21-wk Reproduction	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	NOAEC = 1092.9 mg a.i./kg diet NOAEL = 82.5 mg a.i./kg bw/day LOAEC > 1092.9 mg a.i./kg diet LOAEL > 82.5 mg a.i./kg bw/day No treatment related/biologically relevant effects up to the highest test dose.	N/A	Acceptable	3349487
Mallard duck, *Anas platyrhynchos*	5-d Dietary	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	LC_{50} > 5263 mg a.i./kg diet LD_{50} > 1303 mg a.i./kg bw/day No mortality or dose-	Practically non-toxic	Acceptable	3349486

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
			responsive sublethal effects observed up to the highest dose level.			
	21-wk Reproduction	Fluoxapiprolin, Technical grade active ingredient, purity: 94.5%	NOAEC = 938 mg a.i./kg diet NOAEL = 126.3 mg a.i./kg bw/day LOAEC > 938 mg a.i./kg diet LOAEC > 126.3 mg a.i./kg bw/day No treatment related effects up to highest test dose.	N/A	Acceptable	3349489
Canary, *Serinus canaria*	Acute Oral, limit test	Fluoxapiprolin, Technical grade active ingredient, purity: 94.5%	LD_{50} > 2000 mg a.i./kg bw/day No treatment-related effects observed.	Practically non-toxic	Acceptable	3349484
Mammals						
Wistar rats	Acute oral	a.i.	LD_{50} > 5000 mg a.i./kg bw	Practically non-toxic	Acceptable	3349163
		BCS-CS55621 SC 20 End-use product, containing 1.92% w/w a.i.	LD_{50} > 5000 mg End-use product/kg bw **(LD_{50} > 96 mg a.i./kg bw)**	N/A	Acceptable	3349560
Han Wistar rats	2-generation reproduction	a.i.	**Parental-NOAEL = 262**/302 **mg a.i./kg bw/d** **Offspring-NOAEL = 262**/302 **mg a.i./kg bw/d** No evidence of sensitivity of the young up to the highest dose level.	N/A	Acceptable	3349184

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
Wistar rats	Acute oral	BCS-CS55621-BDM-pyrazole (BCS-BP32808) TP, purity: 98.5%	**LD_{50} = 175 mg/kg bw** (C.I.: 29-714) Clinical signs: decreased activity, hunched posture, piloerection, incoordination and cold to touch	Moderately toxic	Acceptable	3349164
	28-day oral	BCS-CS55621-BDM-pyrazole (BCS-BP32808) in 0.5% CMC TP, purity: 98.5%	NOAEL = 2 mg/kg bw/d LOAEL = 5 mg/kg bw/d ≥ 5 mg/kg bw/d - ↓ bwg, ↓ high beam breaks ♂♀; ↑ piloerection and ↓ activity first day of treatment, ↓ motor activity wk 4 (high and low beam breaks), ↓ urea ♂; ↓ bw, ↓ creatinine, ↑ potassium ♀ 12 mg/kg bw/d - ↓ creatinine ♂; ↑ piloerection and ↓ activity first day of treatment, ↓ low beam breaks, ↓ ovarian wts ♀ Recovery was incomplete but did occur.	N/A	Acceptable	3349177
Vascular plants						
Monocots (barley, corn, onion and wheat) and dicots (oilseed rape, cucumber,	21-d Seedling emergence, limit test at 150 g a.i./ha	BCS-CS55621 SC 20 End-use product, 20.13 g a.i./L (1.92% w/w)	Monocot: NOAER = 150 g a.i./ha **IR_{25}/ER_{25}: > 150 g a.i./ha** Dicot: NOAER: < 150 g a.i./ha LOAER: > 150 g a.i./ha **IR_{25}/ER_{25} > 150 g a.i./ha**	N/A	Acceptable	3349679

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Study acceptability	PMRA No.
soybean, sugar beet, sunflower, and tomato)			Inhibition effect on sunflower survival (8%) and oilseed rape seedling height (6.3%)			
Oilseed rape, *Brassica napus*	21-d Seedling emergence	BCS-CS55621 SC 20 End-use product, 20.85 g a.i./L (1.99% w/w)	NOAEC = 150 g a.i./ha IR_{25}/ER_{25} > 150 g a.i./ha No effects on any endpoints	N/A	Acceptable	3349681
Monocots (barley, corn, onion and wheat) and dicots (oilseed rape, cucumber, soybean, sugar beet, sunflower, and tomato)	21-d vegetative vigor, limit test at 150 g a.i./ha	BCS-CS55621 SC 20 End-use product, 20.13 g a.i./L (1.92% w/w)	All species: NOAER = 150 g a.i./ha IR_{25}/ER_{25}: > 150 g a.i./ha No effects on any endpoints	N/A	Acceptable	3349680

Table 19 Effects of fluoxapiprolin, its formulation and transformation products on aquatic organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
Fresh water species						
Daphnia magna	48-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity 94	**EC_{50} > 0.90 mg a.i./L** (mean measured) No dose-response relationships were observed for immobilization (3–7%) and	Non-toxic up to the limit of functional solubility	Acceptable	3349528

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			sublethal effects included decreased frequency of antennae movements and daphnids being trapped at the surface (0–15%).			
	48-h Acute, static	End-use product, BCS-CS55621 SC 20 G End-use product, 20.13 g a.i./L (1.92% w/w)	EC_{50}: > 1.735 mg End-use product/L (90.1 mg a.i./L) (mean measured) No immobilization and sublethal effects were observed at the highest test concentration.	Non-toxic up to the limit of functional solubility	Acceptable	3349671
	21-d Chronic, static-renewal	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	**NOAEC = 0.032 mg a.i./L** LOAEC > 0.102 mg a.i./L For the most sensitive endpoint of number of live offspring.	N/A	Acceptable	3349427
	48-h acute, static-renewal	BCS-CS55621-BDM-pyrazole (CS-BP32808) TP, purity 99.5%	EC_{50}: = 42 mg/L (TWA) 95% C.I.: 28–78 mg/L Based on immobilization. No sublethal effects observed.	Slightly toxic	Acceptable with limitations 3/7 test concentrations were measured, and the true EC_{50} lies between the analytically verified concentrations of 8.8 and 82 mg/L.	3349419

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
	48-h acute, static-renewal, limit test	BCS-CS55621-pyrazole acetic acid (BCS-CC26101) TP, purity 99.6%	EC_{50}: > 102 mg/L (mean measured) No immobilization or sublethal effects.	Practically non-toxic	Acceptable	3349420
	48-h acute, static	BCS-CS55621-desmesyl (BCS-CS15122) TP, purity 85.5%	EC_{50}: > 3.90 mg/L (mean measured) No immobilization or sublethal effects at the highest test concentration.	Non-toxic up to the limit of functional solubility	Acceptable	3349421
	48-h acute, static	BCS-CS55621-lactam (BCS-DA63612) TP, purity: 98.6%	**EC_{50}: > 0.658 mg/L** (mean measured) (equivalent to 0.94 mg a.i./L) No immobilization or sublethal effects at the highest test concentration.	Non-toxic up to the limit of functional solubility	Acceptable	3349422
	48-h acute, static	BCS-CS55621-piperidine (tested as HCl salt; BCS-CU97237) TP, purity: 97.2%	EC_{50}: = 15.9 mg/L (mean measured as salt, equivalent to **14.7 mg/L BCS-CS55621-piperidine**) 95% C.I.: 13.1 – 19.4 mg/L Based on immobilization. No sublethal effects observed.	Slightly toxic	Acceptable	3349423
	48-h acute, static, limit test	BCS-CS55621-thiazole acid (tested as sodium salt, BCS-DH17585) TP, purity:	EC_{50}: > 98.9 mg/L (mean measured, equivalent to 93.8 mg/L BCS-CS55621-thiazole acid) No immobilization or sublethal	Non-toxic up to the limit of functional solubility	Acceptable	3349424

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
		92.4%	effects.			
	48-h acute, static	BCS-CS55621-4-OH-piperidine (BCS-CY96288) TP, purity: 96.8%	EC_{50}: > 13.9 mg/L (mean measured) Based on immobilization at the highest test concentration.	Non-toxic up to the limit of functional solubility	Acceptable	3349425
	48-h acute, static, limit test	BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260) TP, purity: 98.3%	EC_{50}: > 103 mg/L (mean measured) No immobilization at the highest test concentration; no sublethal effects at any concentration	Practically non-toxic	Acceptable	3349426
Amphipod, *Hyalella azteca*	42-d life-cycle, spiked sediment, intermittent flow-through	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	Sediment: LOAEC: > 80.7 mg a.i./kg NOAEC = 80.7 mg a.i./kg Pore water: LOAEC: > 0.467 mg a.i./L NOAEC = 0.467 mg a.i./L Overlying water: LOAEC: > 0.020 mg a.i./L **NOAEC = 0.020 mg a.i./L** No treatment-related effects on any endpoint (survival, length, dry weight, reproduction) at highest concentration (TWA) tested.	N/A	Acceptable	3349460
Midge, *Chironomus riparius*	48-h acute, static	Fluoxapiprolin Technical grade active	EC_{50}: > 1.01 mg a.i./L (mean measured) NOAEC: 0.537 mg a.i./L	moderately toxic	Acceptable	3349447

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
		ingredient, purity 94.5%	Maximum immobility of 33% and maximum reduced mobility of 15%			
	28-d chronic, spiked water, static	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	Sediment: LOAEC: > 2.68 mg a.i./kg NOAEC = 2.68 mg a.i./kg LOAEC: > 151 mg a.i./kg-OC NOAEC = 151 mg a.i./kg-OC Pore water: LOAEC: > 0.0437 mg a.i./L **NOAEC = 0.0437 mg a.i./L** Overlying water: LOAEC: > 0.246 mg a.i./L NOAEC = 0.246 mg a.i./L No treatment-related effects on emergence and development at highest concentration tested (TWA based).	N/A	Acceptable	3349462
Midge, *Chironomus riparius*	28-d chronic, spiked sediment, static	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	Sediment: LOAEC: 103 mg a.i./kg NOAEC = 57.5 mg a.i./kg LOAEC: 5800 mg a.i./kg-OC NOAEC = 3250 mg a.i./kg-OC Pore water: LOAEC: 0.117 mg a.i./L NOAEC = 0.0618 mg a.i./L Overlying water: LOAEC: 0.235 mg a.i./L	N/A	Acceptable	3349463

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			NOAEC = 0.104 mg a.i./L Endpoints affected were development rates (male, female and combined) (TWA based).			
Midge, *Chironomus dilutus*	48-d life-cycle, spiked sediment, intermittent flow-through	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	Sediment: LOAEC: > 61.5 mg a.i./kg NOAEC = 61.5 mg a.i./kg LOAEC: > 4700 mg a.i./kg-OC NOAEC = 4700 mg a.i./kg-OC Pore water: LOAEC: > 0.286 mg a.i./L NOAEC = 0.286 mg a.i./L Overlying water: LOAEC: > 0.0206 mg a.i./L NOAEC = 0.0206 mg a.i./L No treatment-related effects on survival, dry weight or reproduction at highest concentration tested (TWA based).	N/A	Acceptable	3349459
Rainbow trout, *Oncorhynchus mykiss*	96-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	LC_{50} > 1.06 mg a.i./L No effects up to the highest mean-measured concentration (approximately the limit of solubility)	Non-toxic up to the limit of functional solubility	Acceptable	3349470

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
	96-h Acute, static	BCS-CS55621 SC 20 G End-use product, containing 1.92% w/w fluoxapiprolin)	LC_{50} > 1.81 mg a.i./L No effects up to the highest mean-measured concentration	Non-toxic up to the limit of functional solubility	Acceptable	3349672
Fathead minnow, *Pimephales promelas*	96-h Acute, static, limit test	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	**LC_{50} > 0.94 mg a.i./L** No effects at the mean-measured test concentration (limit of solubility)	Non-toxic up to the limit of functional solubility	Acceptable	3349471
	21-d short-term reproduction, flow-through	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	NOAEC ≥ 0.91 mg a.i./L No effects at the highest mean-measured concentration. Note: the results from this study is to be used qualitatively in risk assessment since from an EDC perspective, use of a NOAEC from a short-term reproductive test is not recommended.	N/A	Acceptable with limitations A short-term screening test, which produced insufficient data to determine reproduction endpoints with certainty.	3349434
	35-d ELS, flow-through	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	**NOAEC ≥ 0.91 mg a.i./L** LOAEC > 0.91 mg a.i./L No effects at the highest mean-measured concentration	N/A	Acceptable	3349475

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
Amphibian, *Xenopus laevis*	43-d (NF62) metamorphosis assay, flow-through	Fluoxapiprolin Technical grade active ingredient, purity 94.5%, w/w	No endpoints were derived. It is a Tier-I screening test. No apparent treatment-related histopathologic effects in the thyroid glands up to 0.83 mg a.i./L on Day 7 and Day 43 (NF62).	NA	Acceptable with limitations The study did not produce endpoints	3349433
Diatom, *Navicula pelliculosa*	96-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity 94.5%, w/w	Yield and Growth rate: IC_{50} > 0.99 mg a.i./L NOAEC = 0.25 mg a.i./L Area Under the Curve: IC_{50} > 0.99 mg a.i./L NOAEC = 0.99 mg a.i./L (endpoints based on initial measured concentrations) The most sensitive endpoint was yield (reduced by 23% at 0.48 mg a.i./L but no effects at 0.99 mg a.i./L).	N/A	Acceptable with limitations Not all validity criteria were met	3349490
Cyanobacterium, *Anabaena flos-aquae*	96-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity 94.5%, w/w	Yield, Growth rate and Area under the curve: IC_{50}: > 1.1 mg a.i./L NOAEC: 1.1 mg a.i./L (endpoints were based on initial measured concentrations)	N/A	Acceptable	3349514
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity 94.5%,	Yield **IC_{50}: > 0.91 mg a.i./L (empirical)** **IC_{05}: 0.398 (95% C.I.: 0.260–0.520) mg a.i./L**	N/A	Acceptable	3349492

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
		w/w	NOAEC: 0.233 mg a.i./L Growth rate IC_{50}: > 0.91 mg a.i./L (empirical) IC_{05}: 1.20 (95% C.I.: 0.947–1.46) mg a.i./L NOAEC: 0.233 mg a.i./L Area under the curve IC_{50}: > 0.91 mg a.i./L (empirical) IC_{05}: 0.467 (95% C.I.: 0.293–0.598) mg a.i./L NOAEC: 0.470 mg a.i./L Endpoints were based on initial measured concentrations. Calculated IC_{50} values were extrapolated well beyond the highest mean-measured test concentration and are uncertain and will not be used for risk assessment.			
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621 SC 20 G End-use product, containing 1.92% w/w fluoxapiprolin	Yield IC_{50}: > 2.03 mg a.i./L IC_{05}: 0.627 mg a.i./L (95% C.I.: 0.48–0.75 mg a.i./L) NOAEC < 0.12 mg a.i./L Growth rate IC_{50}: > 2.03 mg a.i./L NOAEC = 0.237 mg a.i./L	N/A	Acceptable with limitations due to instability of the test item at low range and turbidity at high end of the test	3349677

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			Area under the curve IC_{50}: > 2.03 mg a.i./L NOAEC = 0.237 mg a.i./L Note: the endpoints were based on initial measured concentrations.		concentrations	
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-BDM-pyrazole (BCS-BP32808) TP, purity: >99.9% w/w	Yield IC_{50}: 27.8 mg/L (95% C.I.: 25.9–29.8 mg/L) NOAEC: 3.05 mg/L Growth rate IC_{50}: 75.6 mg/L (95% C.I.: 74.3–76.9 mg/L) NOAEC: 3.05 mg/L Area under the curve IC_{50}: 29.4 mg/L (95% C.I.: 26.5–32.5 mg/L) NOAEC: 9.38 mg/L (endpoints were based on initial measured concentrations)	N/A	Acceptable with limitations due to large pH variation (4.7-10.0)	3349494
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-Pyrazole acetic acid (BCS-CC26101) TP, purity: 99.6% w/w	Yield and Growth rate IC_{50}: > 112 mg/L NOAEC = 112 mg/L Area under the curve IC_{50}: > 112 mg/L	N/A	Acceptable	3349495

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			NOAEC: 3.25 mg/L (endpoints were based on mean measured concentrations) Note: maximum inhibition occurred at the 3rd as well as highest dose levels at 11%.			
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-desmesyl (BCS-CS15122) TP, purity: 85.5% w/w	Yield IC_{50}: 2.6 mg a.i./L (95% C.I.: 2.4–2.8 mg a.i./L) NOAEC: 1.0 mg a.i./L Growth rate IC_{50}: 4.2 mg a.i./L (95% C.I.: 4.1–4.2 mg a.i./L) NOAEC: 1.0 mg a.i./L Area under the curve IC_{50}: 2.3 mg/L (95% C.I.: 2.2–2.5 mg/L) NOAEC: 0.51 mg/L (endpoints were based on initial measured concentrations)	N/A	Acceptable with limitations due to instability of the test item and large pH drift	3349505
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-lactam (BCS-DA63612) TP, purity: 98.6% w/w	Yield, Growth rate and Area under the curve **IC_{50}: > 0.537 mg/L** NOAEC: 0.537 mg/L (endpoints were based on mean-measured	N/A	Acceptable	3349508

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			concentrations) No endpoints affected (promotion of growth in all treatment levels).			
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-piperidine, HCl salt (BCS-CU97237) TP, purity: 97.2% w/w	Yield IC_{50}: 2.12 mg/L (95% C.I.: 1.78–2.51 mg/L) NOAEC: 0.314 mg/L Growth rate IC_{50}: 10.3 mg/L (95% C.I.: 9.04–11.8 mg/L) NOAEC: 0.314 mg/L Area under the curve IC_{50}: 2.72 mg/L (95% C.I.: 2.28–3.25 mg/L) NOAEC: 0.314 mg/L (endpoints were based on initial measured concentrations)	N/A	Acceptable	3349509
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-thiazole acid (as BCS-DH17585, sodium salt) TP, purity: 92.4% w/w	Yield, Growth and Area under the curve IC_{50}: > 94 mg/L NOAEC = 94 mg/L (endpoints were based on mean measured concentrations) Note: no effects up to the highest test concentration.	N/A	Acceptable	3349510

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260) TP, purity: 98.3% w/w	Yield IC_{50}: > 109 mg/L (EFED reported IC_{50} = 141 mg/L with 95% C.I. of 119–167 mg/L, extrapolated beyond the test concentration range of 1.01–109 mg/L) NOAEC: 33.7 mg/L Growth rate IC_{50}: > 109 mg/L (95% C.I.: N/A) NOAEC: 33.7 mg/L Area under the curve IC_{50}: > 109 mg/L (EFED reported IC_{50} = 201 mg/L with 95% C.I. of 124–326 mg/L, extrapolated beyond the test concentration range of 1.01-109 mg/L) NOAEC: 33.7 mg/L (endpoints were based on initial measured concentrations)	N/A	Acceptable with limitations due to uncertainty with the endpoints and large pH drift.	3349512
Green algae, *Pseudokirchneriella subcapitata*	96-h Acute, static	BCS-CS55621-4-OH piperidine (BCS-CY96288) TP, purity: 96.8% w/w	Yield IC_{50}: 12.4 mg/L (95% C.I.: 11.5 – 13.3 mg/L) NOAEC: 3.43 mg/L Growth rate IC_{50}: > 14.4 mg/L	N/A	Acceptable	3349515

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			(EFED reported IC_{50} = 33.7 mg/L with 95% C.I. of 28.6 – 39.7 mg/L, extrapolated beyond the test concentration range of 0.837-14.4 mg/L) NOAEC: 3.43 mg/L Area under the curve IC_{50}: 13.1 mg/L (95% C.I.: 12.3 – 13.9 mg/L) NOAEC: 3.43 mg/L (endpoints were based on mean measured concentrations)			
Vascular plant, duckweed, *Lemna gibba*	7-d acute, static	Fluoxapiprolin Technical grade active ingredient, purity: 94.5% w/w	**IC_{50} > 0.952 mg a.i./L** NOAEC = 0.952 mg a.i./L (endpoints were based on mean measured concentrations.) No dose-responsive effects were observed.	N/A	Acceptable	3349518
	7-d acute, static	BCS-CS55621 SC 20 G End-use product, containing 1.92% w/w fluoxapiprolin	IC_{50} > 1.43 mg a.i./L NOAEC = 1.43 mg a.i./L (endpoints were based on mean measured concentrations. The End-use product was unstable under all dose levels and the two highest test concentrations were turbid.) No dose-responsive effects were observed.	N/A	Acceptable with limitations due to uncertainty of test concentrations.	3349682

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
Marine/Estuarine species						
Amphipod, *Leptocheirus plumulosus*	28-d life-cycle, spiked sediment, intermittent renewal	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	Sediment: LOAEC: > 81.1 mg a.i./kg NOAEC = 81.1 mg a.i./kg LOAEC: > 23000 mg a.i./kg-OC NOAEC = 23000 mg a.i./kg-OC Pore water: LOAEC: > 0.120 mg a.i./L **NOAEC = 0.120 mg a.i./L** Overlying water: LOAEC: >0.0430 NOAEC = 0.0430 mg a.i./L No significant effects (survival, dry weight and reproduction) were determined at the highest test concentration (TWA).	N/A	Acceptable	3349451
Crustacean, mysid shrimp, *Americamysis bahia*	96-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	**LC_{50} > 0.85 mg a.i./L** Based on mean-measured 25% mortality occurred at the highest test concentration	Non-toxic up to the limit of functional solubility	Acceptable with limitations due to instability of the test compound	3349430
	28-day life cycle, flow-through	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	**NOAEC: 0.14 mg a.i./L** LOAEC: 0.29 mg a.i./L Based on TWA The most sensitive endpoint is	N/A	Acceptable	3349542

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	Study acceptability	PMRA No.
			number of offspring/female and body length for both sex			
Mollusk, Eastern oyster, *Crassostrea virginica*	96-h Acute, Static-renewal	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	**IC_{50}: > 0.75 mg a.i./L** (shell deposition) No dose-responsive effects were observed up to the highest mean measured concentrations.	Non-toxic up to the limit of functional solubility	Acceptable with limitations due to poor controls and unstable test concentrations	3349431
Marine diatom, *Skeletonema costatum*	96-h Acute, static	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	**IC_{50} > 1.0 mg a.i./L** NOAEC = 0.53 mg a.i./L (endpoints based on initial measured) Endpoints affected: yield, growth rate, and area under the curve (28% at the highest test concentration)	N/A	Acceptable	3349516
Sheepshead minnow, *Cyprinodon variegatus*	96-h Acute, limit, static	Fluoxapiprolin Technical grade active ingredient, purity: 94.5%	**LC_{50} > 0.93 mg a.i./L** NOAEC = 0.93 mg a.i./L (based on mean-measured) No mortality and toxic effects	Non-toxic up to the limit of functional solubility	Acceptable	3349472
	34-d ELS, flow-through	Fluoxapiprolin Technical grade active ingredient, purity 94.5%	**NOEC = 0.23 mg a.i./L** (based on mean-measured) Endpoints affected: total length and dry weight	N/A	Acceptable	3646953

[a] USEPA classification, where applicable. Because of the low solubility, even when using solvents, acute toxicity classifications remain uncertain for many of the studies. These are indicated in the table as "nontoxic up to the functional solubility limit" in other words, the apparent solubility under test conditions, when no lethal or sublethal effects were observed at the tested concentrations.

Table 20 Parameters used in the risk assessment for fluoxapiprolin

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Effects metric	LOC
Terrestrial species						
Earthworm, *Eisenia fetida* or *Eisenia andrei*	Acute – End-use product	14-d LC_{50}	> 1000 mg End-use product/kg soil dw (> 19.2 mg a.i./kg soil dw)	2	> 500 mg End-use product/kg soil dw (> 9.6 mg a.i./kg soil dw)	1
	Reproduction – End-use product	56-d NOEC	≥ 1000 mg End-use product/kg soil dw (≥ 19.2 mg a.i./kg soil dw)	1	≥ 1000 mg End-use product/kg soil dw (≥ 19.2 mg a.i./kg soil dw)	1
Honey bee, *Apis mellifera*	Acute contact, adults – a.i.	48-h LD_{50}	> 100 µg a.i./bee	1	> 100 µg a.i./bee	0.4
	Acute oral, adults – End-use product	96-h LD_{50}	42.3 µg a.i./bee	1	42.3 µg a.i./bee	0.4
	Chronic oral, adults – End-use product	10-d NOAED	12 µg a.i./bee/d	1	12 µg a.i./bee/d	1
	Chronic oral, larvae – a.i.	8-d LD_{50}	> 18.5 µg a.i./larva/d	1	> 18.5 µg a.i./larvae/d	1
	Chronic oral, larvae – End-use product	22-d NOAED	4.8 µg a.i./larva/d	1	4.8 µg a.i./larva/d	1
Bumble bees, *Bombus terrestris*	Acute oral, adults – End-use product	48-h LD_{50}	> 117.08 µg a.i./bee	1	> 117.1 µg a.i./bee	0.4
	Acute contact, adults – End-use product	48-h LD_{50}	> 100 µg a.i./bee	1	> 100 µg a.i./bee	0.4
Predatory mite	Contact, glass plates – End-use product	7d - LR_{50}	> 60 g a.i./ha	1	> 60 g a.i./ha	2
		14-d NOER	≥ 60 g a.i./ha	1	≥ 60 g a.i./ha	1
Parasitic wasp	Contact, glass	48-h LR_{50}	> 60 g a.i./ha	1	> 60 g a.i./ha	2

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Effects metric	LOC
	plates – End-use product	14-d NOER	≥ 60 g a.i./ha	1	≥ 60 g a.i./ha	1
Soil mites or collembolan	Contact – End-use product	14-d NOEC/ 28-d NOEC	≥ 1000 g End-use product/ kg soil dw (≥ 19.2 mg a.i./kg soil dw)	1	≥ 1000 g End-use product/ kg soil dw (≥ 19.2 mg a.i./kg soil dw)	1
Collembolan	Contact – TP (BCS-BP32808)	28-d LC_{10}	8.1 mg/kg soil dw	1	8.1 mg/kg soil dw	1
Birds	Acute oral – End-use product	14-d LD_{50}	> 2000 mg End-use product/kg bw (> 38.8 mg a.i./kg bw)	10	> 200 mg End-use product/kg bw (> 3.88 mg a.i./kg bw)	1
	Acute dietary – a.i.	5-d LD_{50}	> 964 mg a.i./kg bw/d	10	> 96.4 mg a.i./kg bw/d	1
	Reproduction – a.i.	21-wk NOAEL	82.5 mg a.i./kg bw/d	1	8.23 mg a.i./kg bw/d	1
Mammals	Acute oral – a.i.	LD_{50}	> 5000 mg a.i./kg bw	10	500 mg a.i./kg bw	1
	Reproduction – a.i.	NOAEL	262 mg a.i./kg bw/d	1	262 mg a.i./kg bw/d	1
	Acute oral – TP (BCS-BP32808)	LD_{50}	175 mg/kg bw	10	17.5 mg/kg bw	1
	28-day oral – TP (BCS-BP32808)	NOAEL	2 mg/kg bw/d	1	2 mg/kg bw/d	1
Terrestrial vascular plants	Seedling emergence	21-d IR_{25}/ER_{25}	> 150 g a.i./ha	1	> 150 g a.i./ha	1
	Vegetative vigour	21-d IR_{25}/ER_{25}	> 150 g a.i./ha	1	> 150 g a.i./ha	1
Freshwater species						
Pelagic arthropods	Acute – a.i.	48-h EC_{50}	> 0.90 mg a.i./L	2	> 0.45 mg a.i./L	1
	Chronic – a.i.	21-d NOAEC	0.032 mg a.i./L	1	0.032 mg a.i./L	1
	Acute – TP (BCS-CS55621-lactam)	48-h EC_{50}	> 0.658 mg/L	2	> 0.33 mg/L	1
Benthic arthropod	Chronic – a.i.	42-d NOAEC	0.020 mg a.i./L	1	0.020 mg a.i./L	1

Organism	Exposure / Test substance	Endpoint	Value	Uncertainty factor[1]	Effects metric	LOC
	(spiked sediment)		(overlying water) 80.7 mg a.i./kg (sediment)		(overlying water) 80.7 mg a.i./kg (sediment)	
	chronic – a.i. (spiked water)	28-d NOAEC	0.0437 mg a.i./L (pore water)	1	0.0437 mg a.i./L (pore water)	1
Freshwater fish	Acute – a.i.	96-h LC_{50}	> 0.94 mg a.i./L	10	> 0.094 mg a.i./L	1
	32-d ELS – a.i.	NOAEC	≥ 0.91 mg a.i./L	1	≥ 0.91 mg a.i./L	1
Amphibians (using fish data as a surrogate) [2]	Acute – a.i.	96-h LC_{50}	> 0.94 mg a.i./L	10	> 0.094 mg a.i./L	1
	Chronic	32-d NOAEC	≥ 0.91 mg a.i./L	1	≥ 0.91 mg a.i./L	1
Freshwater algae	Acute – a.i.	96-h EC_{50}	> 0.91 mg a.i./L	2	> 0.46 mg a.i./L	1
Vascular plant	Acute – a.i.	7-d EC_{50}	> 0.952 mg a.i./L	2	> 0.48 mg a.i./L	1
Marine/Estuarine species						
Amphipod	chronic – a.i. (spiked sediment)	28-d NOAEC	0.120 mg a.i./L (pore water) 0.043 mg a.i./L (overlying water)	2	0.06 mg a.i./L (pore water) 0.022 mg a.i./L (overlying water)	1
Crustacean	Acute – a.i.	96-h LC_{50}	> 0.85 mg a.i./L	2	> 0.43 mg a.i./L	1
	Chronic – a.i.	28-d NOAEC	0.14 mg a.i./L	1	0.14 mg a.i./L	1
Mollusk	Acute – a.i.	96-h IC_{50}	> 0.75 mg a.i./L	2	> 0.38 mg a.i./L	1
Marine fish	Acute – a.i.	96-h LC_{50}	> 0.93 mg a.i./L	10	> 0.093 mg a.i./L	1
	34-d ELS – a.i.	NOAEC	0.23 mg a.i./L	1	0.23 mg a.i./L	1
Marine diatom	Acute – a.i.	96-h IC_{50}	> 1.0 mg a.i./L	2	> 0.5 mg a.i./L	1

Table 21 Screening level risk assessment of fluoxapiprolin and transformation products for earthworms, beneficial arthropods and non-target terrestrial vascular plants

Organism	Substance	Exposure	Effects metrics (mg a.i./kg soil; or g a.i./ha)	Screening EEC (mg a.i./kg soil; or g a.i./ha)	RQ	Exceeded screening LOC?
Earthworm	BCS-CS55621 SC 20	Acute 14-d	$LC_{50}/2 > 9.6$	0.025	< 0.003	No

Organism	Substance	Exposure	Effects metrics (mg a.i./kg soil; or g a.i./ha)	Screening EEC (mg a.i./kg soil; or g a.i./ha)	RQ	Exceeded screening LOC?
	BCS-CS55621 SC 20	Chronic 56-d	NOAEC/1 ≥ 19.2	0.025	< 0.01	No
Predatory mite	BCS-CS55621 SC 20	Acute 7-d	LR_{50}/1 > 60	39.9	< 0.66	No
	BCS-CS55621 SC 20	Chronic 14-d	NOAER/1 ≥ 60	39.9	≤ 0.66	No
Parasitic wasp	BCS-CS55621 SC 20	Acute 48-h	LR_{50}/1 > 60	39.9	< 0.66	No
	BCS-CS55621 SC 20	Chronic 14-d	NOAER/1 ≥ 60	39.9	≤ 0.66	No
Killer mites	BCS-CS55621 SC 20	Chronic 28-d	NOAEC/1 ≥ 19.2	0.055	≤ 0.003	No
	BCS-CS55621-BDM-pyrazole	Chronic 28-d	EC_{10}/1 = 8.1	0.007*	0.001	No
Terrestrial plants	BCS-CS55621 SC 20	21-d seedling	ER_{25}/1 > 150	55.4	< 0.37	No
	BCS-CS55621 SC 20	21-d vegetative vigor	ER_{25}/1 > 150	55.4	< 0.37	No

* EEC for BCS-CS55621-BDM-pyrazole was calculated assuming 100% conversion without dissipation from the parent and adjusted for the molecular weight difference.

Table 22 Screening level risk assessment of fluoxapiprolin for bees

Bee stage	exposure		Effects metrics (µg a.i./bee/day)	Exposure to bee (µg a.i./bee/day)[1]	RQ	Exceeded screening LOC?
Honey bee, adult	Contact	Acute	LD_{50} > 100	0.048	< 0.0005	No
	Oral	Acute	LD_{50} = 42.3	0.572	0.014	No
		Chronic	NOAED = 12	0.572	0.048	No
Honey bee, larvae	Oral	Acute	LD_{50} =18.5	0.243	0.013	No
		Chronic	NOAED = 4.8	0.243	0.051	No

[1] Exposure estimate for bees (µg a.i./bee):
For contact exposure route: application rate (kg a.i./ha) × 2.4 µg a.i./bee per kg a.i./ha
For oral exposure route through foliar application: application rate (kg a.i./ha) × 98 µg a.i./g × consumption rate (0.292 g/day for adult bee, 0.124 g/day for larvae)

Table 23 Screening level risk assessment of fluoxapiprolin for birds and mammals

Exposure	Effects metrics (mg a.i./kg bw/d)	Food guild	Estimated daily intake (mg a.i./kg bw/d)[1]	RQ	Exceeded screening LOC?
Birds - Fluoxapiprolin					
Acute	$LD_{50}/10 > 3.88$	Small insectivore birds	3.23	< 0.83	No
		Medium insectivore birds	2.54	< 0.65	
		Large herbivore birds	1.64	< 0.42	
Dietary	$LD_{50}/10 > 96.4$	Small insectivore birds	3.23	< 0.03	No
		Medium insectivore birds	2.54	< 0.03	
		Large herbivore birds	1.64	< 0.02	
Reproduction	NOAEL/1 = 82.3	Small insectivore birds	3.23	0.04	No
		Medium insectivore birds	2.54	0.03	
		Large herbivore birds	1.64	0.02	
Mammals - Fluoxapiprolin					
Acute	$LD_{50}/10 > 500$	Small insectivore mammals	1.85	< 0.01	No
		Medium herbivore mammals	3.52	< 0.01	
		Large herbivore mammals	1.94	< 0.01	
Reproduction	NOAEL/1 = 262	Small insectivore mammals	1.85	< 0.01	No
		Medium herbivore mammals	3.52	0.01	
		Large herbivore mammals	1.94	< 0.01	
Mammals - BCS-CS55621-BDM-pyrazole[2]					
Acute	$LD_{50}/10 > 17.5$	Small insectivore mammals	0.72	0.04	No
		Medium herbivore mammals	1.37	0.08	
		Large herbivore mammals	0.75	0.04	
Reproduction	NOAEL/1 = 2	Small insectivore mammals	0.72	0.36	No
		Medium herbivore mammals	1.37	0.68	
		Large herbivore mammals	0.75	0.38	

[1] Estimated dietary exposure (EDE) is calculated using the following formula: (FIR/BW) × EEC, where:
FIR: Food Ingestion Rate (Nagy, 1987).
For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:
Passerine Equation (body weight < or = 200 g): FIR (g dry weight/day) = $0.398(\text{BW in g})^{0.850}$

All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g) $^{0.651}$.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235 (BW in g) $^{0.822}$
BW: Generic Body Weight
EEC: Concentration of pesticide on food item based on Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher *et al*. (1994). At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used.
[2] For BCS-CS55621-BDM-pyrazole, it was assumed 100% conversion from fluoxapiprolin with molecular weight adjustment.

Table 24 Screening level risk assessment of fluoxapiprolin for non-target aquatic species

Organism	Exposure	Effects metrics (mg a.i./L)	Screening EEC (mg a.i./L)	RQ	Exceeded screening LOC?
Pelagic arthropods	48-h static	$EC_{50}/2 > 0.45$	0.0068	< 0.02	No
	21-d static-renewal	NOAEC/1 = 0.032	0.0068	0.21	No
	48-h static (BCS-CS55621-lactam)	$EC_{50}/2 > 0.33$	0.014	< 0.04	No
Benthic arthropods	42-d spiked sediments	$NOAEC_{pore\ water}/1 = 0.02$	0.0068	0.34	No
	28-d spiked water	$NOAEC_{overlying\ water}/1 = 0.0437$	0.0068	0.16	No
Fresh water fish	96-h static	$LC_{50}/10 > 0.094$	0.0068	< 0.07	No
	32-d flow-through	NOAEC/1 ≥ 0.91	0.0068	≤ 0.01	No
Amphibians (use fish as surrogate)	96-h static	$LC_{50}/10 > 0.094$	0.0363	< 0.39	No
	32-d flow-through	NOAEC/1 ≥ 0.91	0.0363	≤ 0.04	No
Fresh water algae	Acute 96-h static	$EC_{50}/2 > 0.455$	0.0068	< 0.01	No
Fresh water plants	Acute 7-d static	$EC_{50}/2 > 0.476$	0.0068	< 0.01	No
Marine crustacean	Acute 96-h static	$LC_{50}/2 > 0.425$	0.0068	< 0.02	No
	28-d flow-through	NOAEC/1 = 0.14	0.0068	0.05	No
Marine amphipod	28-d spiked sediments	$NOAEC_{overlying\ water}/1 = 0.043$	0.0068	0.16	No
		$NOAEC_{pore\ water}/1 = 0.12$	0.0068	0.057	No
Mollusk	96-h static-renewal	$EC_{50}/2 > 0.375$	0.0068	< 0.02	No

Organism	Exposure	Effects metrics (mg a.i./L)	Screening EEC (mg a.i./L)	RQ	Exceeded screening LOC?
Marine fish	96-h static	$LC_{50}/10 > 0.093$	0.0068	< 0.07	No
	34-d flow-through	NOAEC/1 = 0.23	0.0068	0.03	No
Marine diatom	96-h static	$EC_{50}/2 > 0.5$	0.0068	< 0.01	No

Table 25 List of supported uses

Supported use claims for Xivana Prime
Crops: Brassica head and stem vegetables (Crop Group 5-13) **Disease claim:** Control of downy mildew (*Peronospora parasitica* and *P. brassicae*) **Crops:** Bulb vegetables (Crop Group 3-07) **Disease claim:** Control of downy mildew (*Peronospora destructor*) **Crops:** Cucurbit vegetables (Crop Group 9) **Disease claims:** Control of downy mildew (*Pseudoperonospora cubensis*), suppression of phytophthora blight (*Phytophthora capsici*) **Crops:** Fruiting vegetables (Crop Group 8-09) **Disease claims:** Control of late blight (*Phytophthora infestans*) and pepper downy mildew (*Peronospora tabacina*), suppression of phytophthora blight (*Phytophthora capsici*) **Crops:** Leafy vegetables (Crop Group 4-13) **Disease claim:** Control of downy mildew (*Bremia lactucae* and *Peronospora farinosa*) **Crops:** Leafy petiole vegetables (Crop Subgroup 22B) **Disease claim:** Control of downy mildew (*Peronospora umbellifarum*) **Rate:** 0.75 – 1.0 L/ha (15 – 20 g a.i./ha) **Application timing:** Begin applications preventatively. Use the higher rate when disease pressure is severe. **Number of applications**: Do not exceed 60 g of active ingredient (fluoxapiprolin) per hectare per year (3 L/ha/year). Make applications on a 7- to 14-day interval. **Application method:** Ground application.

Supported use claims for Xivana Prime
Use of adjuvant: A non-ionic surfactant at 0.125% v/v may be added to Xivana Prime for improved efficacy. **Comments:** To limit the potential for development of disease resistance to this fungicide class, do not make more than 2 sequential applications of Xivana Prime or any Group 49 containing fungicide before rotating with a fungicide from a different Group.
Crops: Grape and Amur river grape **Disease claim:** Control of downy mildew (*Plasmopara viticola*) **Rate:** 0.75 – 1.0 L/ha (15 – 20 g a.i./ha) **Application timing:** Begin applications preventatively. Use the higher rate when disease pressure is severe. **Number of applications**: Do not exceed 40 g of active ingredient (fluoxapiprolin) per hectare per year (2 L/ha/year). Make applications on a 10-day interval. **Application method:** Ground application. **Use of adjuvant:** A non-ionic surfactant at 0.125% v/v may be added to Xivana Prime for improved efficacy. **Comments:** To limit the potential for development of disease resistance to this fungicide class, do not make more than 2 sequential applications of Xivana Prime or any Group 49 containing fungicide before rotating with a fungicide from a different Group.
Crop: Potato **Disease claim:** Control of late blight (*Phytophthora infestans*) **Rate:** 0.75 – 1.0 L/ha (15 – 20 g a.i./ha) **Application timing:** Begin applications preventatively. Use the higher rate when disease pressure is severe. **Number of applications**: Do not exceed 60 g of active ingredient (fluoxapiprolin) per hectare per year (3 L/ha/year). Make applications on a 7- to 14-day interval. **Application method:** Ground and aerial application. **Use of adjuvant:** A non-ionic surfactant at 0.125% v/v may be added to Xivana Prime for improved efficacy. **Comments:** To limit the potential for development of disease resistance to this fungicide class, do not make more than 2 sequential applications of Xivana Prime or any Group 49 containing fungicide before rotating with a fungicide from a different Group.

Table 26 Toxic Substances Management Policy considerations - Comparison to TSMP track 1 criteria

TSMP track 1 criteria	TSMP track 1 criterion value		Active ingredient endpoints	Transformation products 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** for aerobic soil (DT_{50} 13.6-92.9 d, n=13) **Yes** for anaerobic soils (DT_{50} 260-367 d, n=2)	**No** for BCS-BP32808 (DT_{50} 3.4-36 d); BCS-CC2601 (DT_{50} 0.7-1.1 d); BCS-CZ38260 (DT_{50} 5.0-10.4 d); **Yes in some soils:** for BCS-DG91934 (DT_{50} 130-214 d, 1/4 met); BCS-DC1250 (DT_{50} 68-389 d, 2/4 met); **Yes** for BCS-DA63612 (DT_{50} 229-315)
	Water	Half-life ≥ 182 days	**No**, aerobic Whole System (DT_{50} 17.7-39 d); anaerobic Whole System (DT_{50} 110-134 d)	Not required
	Sediment	Half-life ≥ 365 days		
	Air	Half-life ≥ 2 days, or evidence of atmospheric transport to remote regions such as the Arctic	Not determined. The AOPWIN (v1.92) model is not suited for predicting the atmospheric half-life of fluoxapiprolin given the large fraction expected to be sorbed to airborne particles.	Not required
Bioaccumulation[4]	Log K_{ow} ≥ 5		No, Log K_{ow} = 3.4	**No**, Log K_{ow} ranges from <1 to 2.9 Specifically for the 3 TPs with persistent concern, Log K_{ow} in pH range of 5 to 9 were: BCS-DG91934 (-1.4 to -0.7); BCS-DC1250 (-1.6 to 1.4); BCS-DA63612 (1.4 to 1.5)
	BCF ≥ 5000		No, 25 L/kg	Not Required

TSMP track 1 criteria	TSMP track 1 criterion value	Active ingredient endpoints	Transformation products endpoints
	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.

[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

Fluoxapiprolin is an active ingredient that is concurrently being registered in Canada and the United States for use on tuberous and corm vegetables (CSG 1C), bulb vegetables (CG3-07), leafy vegetables (CG4-13), brassica vegetables (CG5-13), fruiting vegetables (CG8-09), cucurbit vegetables (CG9), small fruits vine climbing except fuzzy kiwifruit (CSG 13-07F), and leaf petioles vegetables (CSG22B) as primary crops and in/on strawberries as a rotational crop. The MRLs proposed for fluoxapiprolin in Canada are the same as corresponding tolerances to be promulgated in the United States, except for certain commodities, in accordance with Table 1, for which differences in MRLs/tolerances may be due to different legislative requirements.

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

Currently, there are no Codex MRLs[10] listed for fluoxapiprolin in or on any commodity on the Codex Alimentarius Pesticide Index website.

Table 1 compares the MRLs proposed for fluoxapiprolin in Canada with corresponding American tolerances.

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

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)
Strawberries	0.01	Not established
Eggs; milk; fat, meat and meat byproducts of cattle, goats, hogs, horses, poultry and sheep	0.01	Not established

MRLs may vary from one country to another for a number of reasons, including differences in legislative requirements, pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data.

[10] 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
3349115	2021, Fluoxapiprolin (BCS-CS55621) - Description of the manufacturing process of the technical grade active substance for USA and Canada, DACO: 2.11.1,2.11.2,2.11.3
3349118	2019, Fluoxapiprolin (BCS-CS55621) - Technical grade active substance - Discussion on the formation of impurities (specification no. 102000031171), DACO: 2.11.4 CBI
3349120	2018, Determination of BCS-CS55621 in fluoxapiprolin (BCS-CS55621) technical grade and pure active substance by high performance liquid chromatography (HPLC), DACO: 2.13.1 CBI
3349121	2019, Determination of the [CBI removed] in technical grade or pure fluoxapiprolin (BCS-CS55621) by [CBI removed], DACO: 2.13.1 CBI
3349122	2019, Determination of the [CBI removed] in technical grade or pure fluoxapiprolin (BCS-CS55621) by [CBI removed], DACO: 2.13.1 CBI
3349123	2019, Validation of the analytical method AM049317FP2 for the determination of the active ingredient fluoxapiprolin (BCS-CS55621) in technical grade or pure fluoxapiprolin (BCS-CS55621) by high performance liquid chromatography (HPLC), DACO: 2.13.1 CBI
3349124	2019, Validation of the analytical method AM053519FP1 - Determination of the [CBI removed] in technical grade or pure fluoxapiprolin (BCS-CS55621) by [CBI removed], DACO: 2.13.1 CBI
3349125	2019, Validation of the analytical method AM053419FP1 - Determination of the [CBI removed] in technical grade or pure fluoxapiprolin (BCS-CS55621) by [CBI removed], DACO: 2.13.1 CBI
3349126	2019, Material accountability of technical fluoxapiprolin (BCS-CS55621), DACO: 2.13.2,2.13.3,2.13.4 CBI
3349127	2018, Spectral data (UV / VIS, IR, 1H-NMR, 13C-NMR, MS) and molar extinction coefficients of BCS-CS55621, pure substance, DACO: 2.13.2,2.14.12 CBI
3349128	2015, BCS-CS55621, pure substance: Physical characteristics colour, physical state and odour, DACO: 2.14.1,2.14.2,2.14.3 CBI
3349129	2019, Fluoxapiprolin (BCS-CS55621), technical substance: Physical characteristics colour, physical state and odour, DACO: 2.14.1,2.14.2,2.14.3 CBI
3349130	2016, BCS-CS55621, pure substance: Melting point, boiling point, thermal stability, DACO: 2.14.4,2.14.5 CBI
3349131	2019, Melting point and boiling point - Fluoxapiprolin (BCS-CS55621), technical substance, DACO: 2.14.4,2.14.5 CBI

PMRA Document Number	Reference
3349132	2015, BCS-CS55621, pure substance: Relative density, DACO: 2.14.6 CBI
3349133	2019, Fluoxapiprolin (BCS-CS55621), technical substance: Relative density, DACO: 2.14.6 CBI
3349134	2015, Amendment no 1 to study report PA15/005 - BCS-CS55621, pure substance: Solubility in distilled water (column elution method), DACO: 2.14.7 CBI
3349135	2016, BCS-CS55621, pure substance: Solubility in organic solvents, DACO: 2.14.8 CBI
3349136	2016, BCS-CS55621, pure substance: Vapour pressure, DACO: 2.14.9 CBI
3349137	2015, BCS-CS55621, pure substance: Dissociation constant in water, DACO: 2.14.10 CBI
3349138	2015, BCS-CS55621, pure substance: Partition coefficients 1-octanol / water at pH 4, pH 7 and pH 9 (HPLC method), DACO: 2.14.11 CBI
3349139	2021, Stability to elevated temperature, metals, and metal ions and corrosion characteristics to plastic containers of fluoxapiprolin (BCS-CS55621), DACO: 2.14.13 CBI
3349140	2019, Metal corrosivity of fluoxapiprolin (BCS-CS55621), technical substance, DACO: 2.14.13 CBI
3349141	2022, Two year storage stability of fluoxapiprolin (BCS-CS55621) - Technical grade active substance, DACO: 2.14.14 CBI
3349142	2016, BCS-CS55621, pure substance: Determination of the pH-value in distilled water, DACO: 2.14.15,830.7000 CBI
3349143	2019, Fluoxapiprolin (BCS-CS55621), technical substance: Determination of the pH-value in distilled water, DACO: 2.14.15,830.7000 CBI
3349312	2022, Fluoxapiprolin 95 TC - Product chemistry evaluation (based on OECD dossier numbering) - Identity, physical and chemical properties, analytical methods, confidential information, DACO: 12.7.2,Document J, Document M
3349313	2022, Fluoxapiprolin 95 TC - Product chemistry evaluation (based on OECD dossier numbering) - Identity, physical and chemical properties, analytical methods, confidential information, DACO: 12.7.2,Document J, Document M
3349324	2021, An analytical method for the determination of residues of BCS-CS55621, and Its metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in soil and sediment using LC/MS/MS, DACO: 8.2.2.1,8.2.2.2
3349325	2021, In house laboratory validation of analytical method for the determination of residues of BCS-CS55621, and Its metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in soil and sediment using LC/MS/MS, DACO: 8.2.2.1,8.2.2.2

PMRA Document Number	Reference
3349326	2022, Independent laboratory validation of "An analytical method for the determination of residues of BCS-CS55621, and its metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in soil and sediment using LC/MS/MS", DACO: 8.2.2.1,8.2.2.2
3349329	2022, Independent laboratory validation of "An analytical method for the determination of residues of BCS-CS55621, and its metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585 in water using LC/MS/MS" with stability data, DACO: 8.2.2.3
3401652	2021, An Analytical Method for the Determination of Residues of BCS-CS55621, and Its Metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCSCZ38260, BCS-BP32808, and BCS-DH17585 in Water Using LC/MS/MS, DACO: 8.2.2.3
3421229	2022, Spectral Data of specified [CBI removed] in technical fluoxapiprolin (BCS-CS55621) for Canada and USA, DACO: 2.13.2 CBI
3421230	2022, Spectral Characterization Data for the Identified Metabolites (BCSCY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101, BCS-CZ38260, BCS-BP32808, and BCS-DH17585) Used in the Validation Studies for Environmental Analytical Methods, DACO: 8.2.2.1,8.2.2.3
3349550	2022, Product chemistry data to support the registration of fluoxapiprolin SC 20 (20 g/L, Xivana), a fungicide product (product identity and composition), DACO: 3.2.1,3.2.2,3.3.1 CBI
3349552	2016, Determination of BCS-CS55621 in formulations - Assay - HPLC, external standard, DACO: 3.4.1 CBI
3349553	2019, Validation of analytical method AM020616MF1- Determination of fluoxapiprolin in the formulation BCS-CS55621 SC 20 (20 g/L), DACO: 3.4.1 CBI
3349554	2019, Storage stability at elevated temperature and cold stability of fluoxapiprolin SC 20 (20 g/L) - Packaging material: HDPE - Final report (14 days), DACO: 3.5.1,3.5.10,3.5.14,3.5.16,3.5.2,3.5.3,3.5.4,3.5.6,3.5.7,3.5.9 CBI
3349555	2021, Shelf life of fluoxapiprolin SC 20 (20 g/L) - Packaging material: HDPE - Final report (2 years), DACO: 3.5.10,3.5.5 CBI
3349556	2018, Safety-relevant data of BCS-CS55621 SC 20 (20 g/L), DACO: 3.5.11,3.5.12,3.5.8 CBI
3349557	2022, Fluoxapiprolin SC 20 (20 g/L): The oxidation, reduction and chemical incompatibility properties, DACO: 3.5.8 CBI
3349558	2022, Statement according packaging material used in storage stability study of fluoxapiprolin SC 20 (20 g/L) - Packaging material: HDPE - Final report, DACO: 3.5.10 CBI
3349559	2021, Waiver summary report for fluoxapiprolin SC 20 (20 g/L, Xivana), end use product, DACO: 3.5.13,3.5.15 CBI

PMRA Document Number	Reference
3349628	2022, Fluoxapiprolin SC 20 (20 g/L) - Product chemistry evaluation (based on OECD dossier numbering) - Identity, physical and chemical properties, analytical methods, confidential information, DACO: 12.7.3,Document J, Document M

2.0 Human and Animal Health

PMRA Document Number	Reference
3349163	2017, BCS-CS55621 - Acute oral toxicity study in male and female rats (Up and down procedure), DACO: 4.2.1
3349164	2020, BCS-BP32808 - Acute oral toxicity study in rats (up and down procedure), DACO: 4.2.1
3349165	2017, BCS-CS55621 - Acute dermal toxicity study in rats, DACO: 4.2.2
3349166	2016, BCS-CS55621 - Acute inhalation toxicity study (nose-only) in the rat, DACO: 4.2.3
3349167	2017, BCS-CS55621 - Acute eye irritation study in rabbits, DACO: 4.2.4
3349168	2017, BCS-CS55621 - Acute skin irritation study in rabbits, DACO: 4.2.5
3349169	2017, BCS-CS55621 - Local lymph node assay in the mouse, DACO: 4.2.6
3349170	2016, BCS-CS55621: 90-day toxicity study in the mouse by dietary administration, DACO: 4.3.1
3349171	2016, BCS-CS55621 - 90-day toxicity study in the rat by dietary administration, DACO: 4.3.1
3349173	2018, 90-day toxicity study by dietary administration in Beagle dogs - BCS-CS55621, DACO: 4.3.2
3349174	2013, BCS-CS55621- Exploratory 28-day toxicity study in the rat by dietary administration, DACO: 4.3.3
3349175	2013, BCS-CS55621:Preliminary 28-day toxicity study in the mouse by dietary administration, DACO: 4.3.3
3349176	2015, BCS-CS55621 - Preliminary 28-day toxicity study in the dog by dietary administration, DACO: 4.3.3
3349177	2019, BCS-BP32808: Toxicity study by oral (gavage) administration to han wistar rats for 4 weeks followed by a 2-week recovery period, DACO: 4.3.3
3349178	2019, BCS-CS55621 - Range-finding assay for toxicity in the mouse by dietary administration, DACO: 4.3.3
3349179	2018, BCS-CS55621 - 28-day dermal toxicity study in Wistar rats, DACO: 4.3.5
3349180	2022, Waiver request of the data requirements for a subchronic inhalation study - Fluoxapiprolin, DACO: 4.3.6
3349181	2020, BCS-CS55621: Carcinogenicity study in the C57BL/6J mouse by dietary administration, DACO: 4.4.3

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3349182	2020, BCS-CS55621: Chronic toxicity and carcinogenicity study in the Wistar rat by dietary administration, DACO: 4.4.4
3349184	2019, BCS-CS55621: Two generation reproductive performance study to the Han Wistar rat by dietary administration, DACO: 4.5.1
3349185	2018, BCS-CS55621: Preliminary study of reproductive performance in the Han Wistar rat by dietary administration, DACO: 4.5.1
3349186	2016, BCS-CS55621 - Developmental toxicity study in the rat by gavage, DACO: 4.5.2
3349187	2015, BCS-CS55621 - Range-finding study for developmental toxicity in the rat by gavage, DACO: 4.5.2
3349188	2018, BCS-CS55621: Study for effects on embryo-fetal development in the New Zealand White rabbit by oral gavage administration, DACO: 4.5.3
3349189	2018, BCS-CS55621: Study for effects on embryo-fetal development in the New Zealand White rabbit by oral gavage administration, DACO: 4.5.3
3349190	2018, BCS-CS55621: Study for effects on embryo-fetal development in the New Zealand White rabbit by oral gavage administration, DACO: 4.5.3
3349191	2017, BCS-CS55621 - Range-finding study for developmental toxicity in the rabbit by gavage, DACO: 4.5.3
3349192	2019, BCS-CS55621: Salmonella typhimurium reverse mutation assay, DACO: 4.5.4
3349193	2017, BCS-CS55621: Salmonella typhimurium reverse mutation assay, DACO: 4.5.4
3349194	2019, BCS-CC26101 - Salmonella typhimurium reverse mutation assay, DACO: 4.5.4
3349195	2020, BCS-CZ38260 - Salmonella typhimurium reverse mutation assay, DACO: 4.5.4
3349196	2018, BCS-BP32808: Salmonella typhimurium reverse mutation assay, DACO: 4.5.4
3349197	2016, Mutagenicity study of BCS-CU97237, technical in the Salmonella typhimurium reverse mutation assay (in vitro), DACO: 4.5.4
3349198	2017, BCS-CS55621: Gene mutation assay in Chinese hamster V79 cells in vitro (V79/HPRT), DACO: 4.5.5
3349199	2019, BCS-BP32808: Gene mutation assay in chinese hamster V79 cells in vitro (V79-HPRT), DACO: 4.5.5
3349200	2019, BCS-CC26101: Gene mutation assay in chinese hamster V79 cells in vitro (V79-HPRT), DACO: 4.5.5
3349201	2020, BCS-CZ38260: Gene mutation assay in chinese hamster V79 Cells in vitro (V79-HPRT), DACO: 4.5.5
3349202	2017, BCS-CS55621: Chromosome aberration test in human lymphocytes in vitro, DACO: 4.5.6
3349203	2018, BCS-BP32808: Micronucleus test in human lymphocytes in vitro, DACO: 4.5.6

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3349204	2019, BCS-CC26101: Micronucleus test in human lymphocytes in vitro, DACO: 4.5.6
3349205	2020, BCS-CZ38260: Micronucleus test in human lymphocytes in vitro, DACO: 4.5.6
3349206	2017, BCS-CS55621: Micronucleus test in human lymphocytes in vitro, DACO: 4.5.6
3349207	2019, BCS-CS55621: Micronucleus test in human lymphocytes in vitro, DACO: 4.5.6
3349208	2018, BCS-CS55621 - Micronucleus assay in bone marrow cells of the mouse, DACO: 4.5.7
3349209	2018, BCS-BP32808 - Micronucleus assay in bone marrow cells of the mouse, DACO: 4.5.7
3349210	2020, BCS-BP32808: In vivo mutation assay at the cII locus in Big Blue¿¿ Transgenic C57BL/6 mice with a 5-day dose range finder, DACO: 4.5.8
3349243	2019, Amendment no.01: [Phenyl-UL-14C]BCS-CS55621 - Absorption, distribution, excretion and metabolism in the rat, DACO: 4.5.9
3349244	2019, [pyrazole-4-14C]BCS-CS55621 - Bioaccumulation in organs and tissues of male and female rats, DACO: 4.5.9
3349245	2018, Amendment no. 1 to final report: [Acetyl-2-14C]BCS-CS55621: Pilot metabolism experiments in male rats, DACO: 4.5.9
3349246	2019, [Pyrazole-4-14C]BCS-CS55621 - Absorption, distribution, excretion and metabolism in the rat, DACO: 4.5.9
3349247	2017, [pyrazole-4-14C]BCS-CS55621: Tissue distribution and excretion of radioactivity in the rat by quantitative whole body autoradiography, DACO: 4.5.9
3349248	2019, BCS-CS55621 : 14-day bioanalytical study in the rat by dietary administration, DACO: 4.5.9
3349249	2019, Amendment no. 01: Metabolic stability and profiling of [thiazolyl-2-14C]fluoxapiprolin (BCS-CS55621) in liver microsomes from human, rat and dog for interspecies comparison, DACO: 4.5.9
3349250	2020, Metabolic stability and profiling of [pyrazole-4-14C]fluoxapiprolin (BCS-CS55621) in liver microsomes from human, rat and dog for interspecies comparison, DACO: 4.5.9
3349251	2020, Metabolic stability and profiling of [phenyl-UL-14C]fluoxapiprolin (BCS-CS55621) in liver microsomes from human, rat and dog for interspecies comparison, DACO: 4.5.9
3349252	2018, BCS-CS55621: Neurotoxicity study by a single oral administration to Han Wistar rats followed by a 14 day observation period, DACO: 4.5.12
3349253	2021, Waiver request of the data requirements for subchronic neurotoxicity studies, DACO: 4.5.13
3349254	2021, Waiver request of the data requirements for immunotoxicity study - Fluoxapiprolin, DACO: 4.5.15,870.78

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3349255	2022, Position paper - Fluoxapiprolin - Justification for not conducting a repeat-dose immunotoxicity study, DACO: 4.5.15,870.78
3349263	2022, Position paper - Fluoxapiprolin - Justification for not conducting a repeat-dose immunotoxicity study, DACO: 4.8
3349264	2013, BCS-CS55621 - Evaluation in the immature rat uterotrophic assay coupled with vaginal opening assessment, DACO: 4.8
3349265	2013, BCS-CS55621 - Evaluation in the weanling rat Hershberger assay coupled with preputial separation assessment, DACO: 4.8
3349266	2019, BCS-CS55621 - Assessment in the H295R steroidogenesis screen - Amendment n¿¿1 to Final Report, DACO: 4.8
3349267	2022, Expert statement - Fluoxapiprolin (BCS-CS55621) - Response to UK Health & Safety Executive (Chemicals Regulation Division) on KMD approach, DACO: 4.8
3349268	2017, Determination of kinetically-derived maximum dose (KMD) for BCS-CS55621 in rats, DACO: 4.8
3349269	2017, Determination of kinetically-derived maximum dose (KMD) of BCS-CS55621 in mice, DACO: 4.8
3349560	2018, BCS-CS55621 SC20: Acute oral toxicity study in male and female rats (up and down procedure), DACO: 4.6.1
3349561	2018, BCS-CS55621 SC 20: Acute dermal toxicity study in rats, DACO: 4.6.2
3349562	2018, BCS-CS55621 SC 20: Acute inhalation toxicity study (nose-only) in the rat, DACO: 4.6.3
3349563	2018, BCS-CS55621 SC 20: Acute eye irritation study in rabbits, DACO: 4.6.4
3349564	2018, BCS-CS55621 SC 20: Acute skin irritation study in rabbits, DACO: 4.6.5
3349565	2018, BCS-CS55621 SC 20: Local lymph node assay in the mouse, DACO: 4.6.6
3395583	2022, BCS-AA10147 - 104-week chronic toxicity combined with carcinogenicity study by the oral (dietary admixture) route in the Wistar rat, DACO: 4.4.4
3473545	2013, BSC-CS55621 Preliminary 28 day toxicity study in the mouse by dietary administration, DACO: 4.8
3473546	2013, BSC-CS55621 Determination by High Performance liquid Chromatography analysis in the canine diet, DACO: 4.3.3
3473547	2013, BSC-CS55621 Stability in Ground Rodent Diet, DACO: 4.8
3502742	2023, Response to clarification PMRA DOC NUMBER 3349246, DACO: 4.8
3502743	2023, dose calculations, DACO: 4.8
3502744	2023, settings, DACO: 4.8
3502745	2023, timecourse, DACO: 4.8
3520615	2023, HCD Rat 2y glandular hyperplasia and polyp 2023-10-31, DACO: 4.4.1,4.4.2
3520616	2023, HCD Rat 2y thyroid C cell tumor 2023-10-31, DACO: 4.4.1,4.4.2

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3520617	2023, RITA Thyroid_gland_Adenoma_C-cell, DACO: 4.4.1,4.4.2
3520618	2023, RITA Thyroid_gland Carcinoma_C-cell, DACO: 4.4.1,4.4.2
3520619	2023, RITA Uterus_Hyperplasia_endometrium_diffuse, DACO: 4.4.1,4.4.2
3520620	2023, RITA Uterus_Hyperplasia_glandular_focal, DACO: 4.4.1,4.4.2
3520621	2023, RITA Uterus_Polyp_endometrial_stromal, DACO: 4.4.1,4.4.2
3521189	2023, Response to Clarification of Historical Control Data , DACO: 4.4.1,4.4.2
3583172	2024, Regulatory Response to the Toxicology 75-day Notice of Deficiencies for Fluoxapiprolin from the PMRA, DACO: 4.4.3,4.4.4,4.5.1,4.5.9,4.8
3583173	2021, Expert opinions on the relevance of thymomas and endometrial changes in the uterus in female rats, DACO: 4.4.4
3583174	2023, Pathology working group review of thymus proliferation epithelial findings from a chronic toxicity and carcinogenicity study, DACO: 4.4.4
3590720	2023, Response to Clarification PMRA DOC NUMBER 3349243, DACO: 4.8
3590721	2023, Spreadsheet calculations, DACO: 4.8
3590722	2023, Settings, DACO: 4.8
3590723	2023, timecourse, DACO: 4.8
3590724	2023, Response to clarification PMRA DOC NUMBER 3349246, DACO: 4.8
3590725	2023, dose calculations, DACO: 4.8
3590726	2023, settings, DACO: 4.8
3590727	2023, timecourse, DACO: 4.8
3590730	2013, Stability in the Ground Rodent Diet, DACO: 4.8
3590731	2024, PRELIMINARY RANGE-FINDING ASSAY FOR DEVELOPMENTAL TOXICITY IN THE RABBIT BY GAVAGE, DACO: 4.8
3591912	2024, Historical Control Data, DACO: 4.8
3605363	2024, Bayer Response to Clarification Questions, DACO: 4.8
3606668	2024, Bayer Response to Clarification question, DACO: 4.8
3349567	2019, BCS-CS55621 SC 20 (20 g/L) - In vitro absorption through rat dermatomed skin using [14C]-BCS-CS55621 (fluoxapiprolin), DACO: 5.8
3349568	2019, BCS-CS55621 SC 20 (20 g/L) - In vitro absorption through human dermatomed skin using [14C]-BCS-CS55621 (fluoxapiprolin), DACO: 5.8
3349569	2019, [14C]-BCS-CS55621 (fluoxapiprolin) - BCS-CS55621 SC 20 (20 g/L) - OECD 427 in vivo dermal penetration study in rat, DACO: 5.8
3349582	2019, Analytical method 01554 for the determination of BCS-CS55621 and its metabolites BCS-CC26101, BCS-BP32808, BCS-DE61185, BCS-DE72760 and BCS-DE72761 in plant by HPLC-MS/MS, DACO: 7.2.1
3349583	2019, An analytical method for the determination of residues of BCS-CS55621, and its metabolites BCS-CC26101, BCS-BP32808, BCS-DE61185, BCS-DE72760 and BCS-DE72761 in crop matrices using LC/MS/MS, DACO: 7.2.1

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3349586	2019, Amendment no. 1: Validation of an enforcement method for the determination of BCS-CS55621 in different matrices of animal origin, DACO: 7.2.2
3349587	2019, Residue analytical enforcement method 01624 for the determination of BCS-CS55621 and its metabolites BCS-DE61185, BCS-DE72761 and BCS-CC26101 in samples of plant origin by LC/MS/MS, DACO: 7.2.2
3349588	2020, Independent laboratory validation of analytical method no. 01624 for the determination of fluoxapiprolin and its metabolites BCS-CC26101, BCS-DE61185 and BCS-DE72761 in/on samples of plant origin, DACO: 171 - 4a,171 - 4c,171 - 4m,171-4a-4b,171-4c-4d,7.2.3A,860.1300,860.1340,860.1360, IIA 4.2.6, IIIA 5.3.1,b,d
3349589	2019, Independent laboratory validation of analytical method no. 01628 for the determination of fluoxapiprolin in/on samples of animal origin, DACO: 171 - 4a,171 - 4c,171 - 4m,171-4a-4b,171-4c-4d,7.2.3A,860.1300,860.1340,860.1360, IIA 4.2.6, IIIA 5.3.1,b,d
3349592	2019, Extraction efficiency testing of the residue analytical method for data gathering for the determination of the relevant residue of BCS-CS55621 in/on plants using radioactive incurred residues, DACO: 7.2.3B
3349593	2019, Storage stability of residues of BCS-CS55621 and its metabolites BCS-CC26101, BCS BP32808, BCS-DE61185, BCS-DE72760 and BCS-DE72761 in tomato (fruit), potato (tuber), grapes (fruit), sunflower (seed) and field peas (dry seed) during deep freeze storage for at least 24 months and determination of the enantiomeric ratio of BCS-CS55621 in tomato, potato, grapes after deep freeze storage for 21 months and in sunflower and field peas after deep freeze storage for 12 months, DACO: 7.3
3349594	2021, Storage stability of BCS-CS55621 and its metabolites BCS-BP32808, BCS-CC26101, BCS-DE72760, BCS-DE72761, BCS-DE61185 in/on plant matrices - Final report, DACO: 7.3
3349150	2020, [Pyrazole-4-^{14}C]BCS-CS55621 - Metabolism in the laying hen, DACO: 6.2
3349151	2019, [Phenyl-UL-^{14}C]BCS-CS55621 - Metabolism in the laying hen, DACO: 6.2
3349152	2019, [Pyrazole-4-^{14}C]BCS-CS55621 - Metabolism in the lactating goat, DACO: 6.2
3349153	2019, [Phenyl-UL-^{14}C]BCS-CS55621 - Metabolism in the lactating goat, DACO: 6.2
3349154	2019, Metabolism of [pyrazole-4-^{14}C]BCS-CS55621 in lettuce, DACO: 6.3
3349155	2019, Metabolism of [phenyl-UL-^{14}C]BCS-CS55621 in lettuce, DACO: 6.3
3349156	2019, Metabolism of [pyrazole-4-^{14}C]BCS-CS55621 in grapes, DACO: 6.3
3349158	2019, Metabolism of [phenyl-UL-^{14}C]BCS-CS55621 in grapes, DACO: 6.3
3349159	2019, Metabolism of [pyrazole-4-^{14}C]BCS-CS55621 in potato, DACO: 6.3
3349160	2019, Metabolism of [phenyl-UL-^{14}C]BCS-CS55621 in potato, DACO: 6.3

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3349597	2021, Magnitude of the residues of fluoxapiprolin in limited rotational crops after spray application of fluoxapiprolin SC 20 (20 g/L) - Soybeans, DACO: 7.4.4
3349598	2021, Magnitude of the residues of fluoxapiprolin in limited rotational crops after spray application of fluoxapiprolin SC 20 (20 g/L) - Turnips, DACO: 7.4.4
3349599	2021, Magnitude of the residues of fluoxapiprolin in limited rotational crops after spray application of fluoxapiprolin SC 20 (20 g/L) - Wheat, DACO: 7.4.4
3349600	2021, Magnitude of the fluoxapiprolin residues in/on strawberry planted 30 days after spray application of BCS-CS55621 SC 020 (20 g/L) in North America, DACO: 7.4.4
3349601	2022, Waiver of the requirement for livestock feeding studies for fluoxapiprolin, DACO: 7.5,7.5.1
3349602	2022, Waiver of the requirement for livestock feeding studies for fluoxapiprolin, DACO: 7.5,7.5.1
3349605	2021, Magnitude of the residues of fluoxapiprolin in/on potatoes after spray application of fluoxapiprolin SC 20 (20 g/L), DACO: 7.4.1,7.4.2
3349606	2021, Magnitude of the residues of fluoxapiprolin in/on grape after spray application of fluoxapiprolin SC 20 (20 g/L), DACO: 7.4.1,7.4.2
3349607	2021, Magnitude of the fluoxapiprolin residues in/on bulb vegetables after spray application of BCS-CS55621 SC020 (20g/L) in North America, DACO: 7.4.1,7.4.2
3349608	2021, Magnitude of the fluoxapiprolin residues in/on brassica vegetables after spray application of BCS-CS55621 SC 020 (20 g/L) in North America, DACO: 7.4.1,7.4.2
3349610	2021, Magnitude of the fluoxapiprolin residues in/on leaf petiole vegetables after spray application of BCS-CS55621 SC 020 (20 g/L) in North America, DACO: 7.4.1,7.4.2
3349611	2021, Magnitude of the residues of fluoxapiprolin in/on cucurbit vegetables after spray application of fluoxapiprolin SC 20 (20 g/L), DACO: 7.4.1,7.4.2
3349612	2022, Magnitude of the fluoxapiprolin residue in/on fruiting vegetables after spray application of BCS-CS55621 SC 20 (20 g/L) in North America, DACO: 7.4.1,7.4.2
3349616	2021, Magnitude of the fluoxapiprolin residues in/on leafy vegetables after spray application of BCS-CS55621 SC 020 (20 g/L) in North America, Part I, DACO: 7.4.1,7.4.2
3349619	2021, Magnitude of the fluoxapiprolin residues in/on leafy vegetables after spray application of BCS-CS55621 SC 020 (20 g/L) in North America, Part 2, DACO: 7.4.1,7.4.2
3349622	2019, Metabolism of [phenyl-UL-^{14}C]BCS-CS55621 in confined rotational crops, DACO: 7.4.3
3349623	2019, Metabolism of [pyrazole-4-^{14}C]BCS-CS55621 in confined rotational crops, DACO: 7.4.3

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3349624	2019, BCS-CS55621 SC 20 - Magnitude of the residue in/on tomato processed commodities, DACO: 7.4.5
3349625	2019, Determination of the residues of BCS-CS55621 in/on table grape and the processed fractions (fruit, stored and raisin) after spraying of BCS-CS55621 SC 020 in the field in Italy, DACO: 7.4.5
3349626	2019, Determination of the residues of BCS-CS55621 in/on potato and the processed fractions (French fries (Br.: chips); concentrate; crisps (Am.: chips); fibre; flakes; peel washed; potato, fried; protein isolate; pulp, dry; starch; tuber with peel, cooked; tuber, baked; tuber, baked, peeled; tuber, cooked; tuber, cooked, peeled; tuber, peeled; tuber, steamed, mashed; tuber, stored; tuber, washed; waste and waste, dried) after Spraying of BCS-CS55621 SC 020 in the Field in Germany, the Netherlands and France (South), DACO: 7.4.5
3349627	2019, Determination of the residues of BCS-CS55621 in/on grape and the processed fractions (fruit, stored; pomace, wet; raw juice; juice; must; wine at bottling and wine at first taste test) after spraying of BCS-CS55621 SC 020 in the field in Germany, DACO: 7.4.5
3473319	2020, Analytical Method N° 01634 for the determination of BCS-CS55621 enantiomers in plant by HPLC-MS/MS, DACO: 7.2.1
3703295	2025, Magnitude of the Residue of Fluoxapiprolin in/on Wheat Planted 30 Days After Spray Application of Fluoxapiprolin SC 20 to Bare Soil in North America – Final report, DACO: 7.4.4

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3349334	2016, [Phenyl-UL-^{14}C]BCS-CS55621: Phototransformation on soil, DACO: 8.2.3.3.1
3349335	2017, [Pyrazole-4-^{14}C]BCS-CS55621: Phototransformation on soil, DACO: 8.2.3.3.1
3349336	2017, [Phenyl-UL-^{14}C]BCS-CS55621: Phototransformation in water, DACO: 8.2.3.3.2
3349338	2017, [Pyrazole-4-^{14}C]BCS-CS55621: Phototransformation in water, DACO: 8.2.3.3.2
3349339	2015, BCS-CS55621: Determination of the quantum yield and assessment of the environmental half-life of the direct photo-degradation in water, DACO: 8.2.3.3.2
3349340	2015, BCS-CS55621: Calculation of the chemical half-life in the troposphere, DACO: 8.2.3.3.3

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3349341	2019, Amendment no. 01: [Phenyl-UL-^{14}C]BCS-CS55621: Aerobic soil metabolism on two US soils, DACO: 8.2.3.4.2
3349342	2018, [phenyl-UL-^{14}C] BCS-CS55621: Aerobic degradation / Metabolism in four soils, DACO: 8.2.3.4.2
3349343	2019, [Pyrazole-4-^{14}C]BCS-CS55621: Aerobic soil metabolism on two US soils, DACO: 8.2.3.4.2
3349344	2017, [pyrazole-^{14}C]BCS-CS55621: Aerobic degradation / Metabolism in four soils, DACO: 8.2.3.4.2
3349345	2019, BCS-CS55621: Aerobic degradation / Metabolism in one soil, DACO: 8.2.3.4.2
3349346	2019, BCS-CS55621-piperidine: Aerobic degradation in four soils, DACO: 8.2.3.4.2
3349347	2017, [acetic acid-2-^{14}C]BCS-CC26101: Aerobic degradation in four soils, DACO: 8.2.3.4.2
3349348	2018, BCS-CZ38260: Aerobic degradation in four soils, DACO: 8.2.3.4.2
3349349	2019, BCS-CS55621-thiazole acid: Aerobic degradation in four soils at 20˚C in the dark, DACO: 8.2.3.4.2
3349350	2019, Amendment no. 01: BCS-BP32808: Aerobic degradation in four soils, DACO: 8.2.3.4.2
3349351	2019, BCS-CS55621-lactam: Aerobic degradation in four soils, DACO: 8.2.3.4.2
3349353	2018, [Phenyl-UL-^{14}C]BCS-CS55621:Anaerobic degradation / metabolism in one soil, DACO: 8.2.3.4.4
3349354	2018, [Pyrazole-4-^{14}C]BCS-CS55621: Anaerobic degradation/metabolism in one soil, DACO: 8.2.3.4.4
3349355	2016, [Phenyl-UL-^{14}C]BCS-CS55621: Aerobic aquatic degradation / metabolism, DACO: 8.2.3.5.4
3349356	2016, Amendment no. 01: [Pyrazole-^{14}C]BCS-CS55621: Aerobic aquatic degradation / Metabolism, DACO: 8.2.3.5.4
3349358	2022, [Phenyl-UL-^{14}C] and [Pyrazole-4-^{14}C]BCS-CS55621: Anaerobic aquatic metabolism in two water/sediment systems - Final report, DACO: 8.2.3.5.6
3480767	2023, [^{14}C]BCS-CS55621: Determination of Adsorption/desorption in three soils, DACO: 8.2.4.2
3349362	2017, [pyrazole-4-^{14}C] BCS-CS55621: Adsorption /desorption in three different soils, DACO: 8.2.4.2
3349364	2017, [acetyl-2-^{14}C] BCS-CY96288: Adsorption/desorption in five different soils, DACO: 8.2.4.2
3349366	2017, BCS-CS55621-piperidine: Adsorption/desorption on four soils, DACO: 8.2.4.2
3349368	2017, [acetic acid-2-14C]BCS-CC26101: Adsorption / Desorption on four soils, DACO: 8.2.4.2

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3349370	2017, BCS-CS55621-lactam: Adsorption / desorption on four soils, DACO: 8.2.4.2
3349372	2019, BCS-BP32808 - Adsorption / Desorption on five soils, DACO: 8.2.4.2
3349375	2019, BCS CS55621-thiazole acid: Adsorption / desorption on four soils, DACO: 8.2.4.2
3349572	2022, Terrestrial field dissipation of BCS-CS55621 in Ontario bare ground soil, 2019 - Final report, DACO: 8.3.2.1
3349573	2022, Terrestrial field dissipation of BCS-CS55621 in Iowa bare ground soil, 2019 - Final Report -, DACO: 8.3.2.2
3349575	2022, Terrestrial field dissipation of BCS-CS55621 in California bare ground soil, 2019 - Final report, DACO: 8.3.2.2
3349576	2022, Terrestrial field dissipation of BCS-CS55621 in Georgia bare ground soil, 2019, DACO: 8.3.2.2
3349577	2022, Terrestrial field dissipation of BCS-CS55621 in Washington bare ground soil, 2019 - Final report, DACO: 8.3.2.2
3349595	2019, Determination of the storage stability of BCS-CS55621 and the metabolites BCS-CY96288, BCS-CU97237, BCS-DA63612, BCS-CC26101 and BCS-CZ38260 in soil for 24 months, DACO: 7.3
3349596	2022, Amendment 01 to 18-month data report - Storage stability of BCS-BP32808 and BCS-DH17585 in soil (18-month data), DACO: 7.3
3349270	2016, BCS-CY96288 (BCS-CS55621-4-OH piperidine): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9 (HPLC-method), DACO: 8.6
3349271	2016, BCS-CY96288 (BCS-CS55621-4-OH piperidine): Water solubility at pH 7 (flask method), DACO: 8.6
3349272	2019, BCS-CS55621-4-OH piperidine - Estimation of vapour pressure, DACO: 8.6
3349273	2016, BCS-CS55621-BCS-CU97237: Partition coefficient 1-octanol / water at pH 7 and pH 10 (shake flask method), DACO: 8.6
3349274	2017, BCS-CU97237 (BCS-CS55621-piperidine (HCl salt)): Partition coefficients 1-octanol / water at pH 5, pH 7 and at pH 9 (shake flask method), DACO: 8.6
3349275	2018, BCS-CU97237 (BCS-CS55621-piperidine (HCl salt)): Water solubility at pH 5, pH 7, pH 8 and pH 10, DACO: 8.6
3349276	2018, BCS-CU97237 (BCS-CS55621-piperidine (HCl salt)): Estimation of the dissociation constant in water, DACO: 8.6
3349277	2019, BCS-CS55621-piperidine - Estimation of vapour pressure, DACO: 8.6
3349278	2017, BCS-CC26101 (BCS-CS55621-pyrazole acetic acid): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9 (shake flask method), DACO: 8.6
3349279	2019, BCS-CS55621-pyrazole acetic acid - Estimation of water solubility, DACO: 8.6
3349280	2019, BCS-CS55621-pyrazole acetic acid - Estimation of vapour pressure, DACO: 8.6

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3349281	2017, BCS-CZ38260 (BCS-CS55621-pyrazole-carboxylic acid): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9 (shake flask method), DACO: 8.6
3349282	2019, BCS-CS55621-pyrazole-carboxylic acid - Estimation of water solubility, DACO: 8.6
3349283	2017, BCS-CZ38260 (BCS-CS55621-pyrazole-carboxylic acid): Dissociation constant in water, DACO: 8.6
3349284	2019, BCS-CS55621-pyrazole-carboxylic acid - Estimation of vapour pressure, DACO: 8.6
3349285	2017, BCS-CS15122 (BCS-CS55621-desmesyl): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9 (HPLC method), DACO: 8.6
3349286	2017, BCS-CS15122 (BCS-CS55621-desmesyl): Water solubility at pH 5, pH 7 and pH 9, DACO: 8.6
3349287	2017, BCS-CS15122 (BCS-CS55621-desmesyl): Dissociation constant in water, DACO: 8.6
3349290	2017, BCS-CS55621-BCS-BP32808: Partition coefficient 1-octanol / water (shake flask method), DACO: 8.6
3349291	2019, BCS-BP32808 (BCS-CS55621-BDM-pyrazole): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9, DACO: 8.6
3349293	2017, BCS-CS55621-BCS-BP32808: Solubility in distilled water (flask method), DACO: 8.6
3349294	2019, BCS-BP32808 (BCS-CS55621-BDM-pyrazole): Water solubility at pH 5, pH 7 and pH 9 (flask method), DACO: 8.6
3349295	2019, BCS-BP32808 (BCS-CS55621-BDM-pyrazole): Dissociation constant in water, DACO: 8.6
3349296	2017, BCS-CS55621-BCS-BP32808: Vapour pressure, DACO: 8.6
3349298	2017, BCS-DA63612 (BCS-CS55621-lactam): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9 (shake flask method), DACO: 8.6
3349299	2017, BCS-DA63612 (BCS-CS55621-lactam): Solubility in distilled water (column elution method), DACO: 8.6
3349300	2019, Fluoxapiprolin (FXN) - Estimation of dissociation constants of BCS-CS55621-lactam, DACO: 8.6
3349301	2019, BCS-CS55621-lactam - Estimation of vapour pressure, DACO: 8.6
3349302	2019, BCS-DH17585 (BCS-CS55621-thiazole acid (Na-salt)): Partition coefficients 1-octanol / water at pH 5, pH 7 and pH 9 (shake flask method), DACO: 8.6
3349303	2019, BCS-DH17585 (BCS-CS55621-thiazole acid (Na-salt)): Water solubility at pH 5, pH 7 and pH 9 (flask method), DACO: 8.6
3349304	2019, BCS-DH17585 (BCS-CS55621-thiazole acid (Na-salt)): Dissociation constant in water, DACO: 8.6
3349305	2019, BCS-CS55621-thiazole acid - Estimation of vapour pressure, DACO: 8.6

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3349306	2016, BCS-CY96288 (BCS-CS55621-4-OH piperidine): Dissociation constant in water, DACO: 8.6
3349307	2017, BCS-CC26101 (BCS-CS55621-pyrazole acetic acid): Dissociation constant in water, DACO: 8.6
3349395	2018, BCS-CS55621 a.s.: Acute toxicity to the earthworm *Eisenia andrei* in artificial soil, DACO: 9.2.3.1
3349653	2019, Fluoxapiprolin (BCS-CS55621) SC 20 (20 g/L): Acute toxicity to earthworms (*Eisenia fetida*) tested in artificial soil, DACO: 9.2.3.1
3349654	2019, BCS-CS55621 SC 20 G: Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.2.3.2
3349388	2019, BCS-CS55621-BDM-pyrazole (BCS-BP32808): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349389	2019, BCS-CS55621-pyrazole acetic acid (BCS-CC26101): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349390	2019, BCS-CS55621-thiazole acid (sodium salt) (BCS-DH17585): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349391	2019, BCS-CS55621-lactam (BCS-DA63612): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349392	2019, BCS-CS55621-4-OH piperidine (BCS-CY96288): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349393	2019, BCS-CS55621-piperidine (HCl salt) (BCS-CU97237): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349394	2019, BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260): Effects on survival, growth and reproduction of the earthworm *Eisenia fetida* tested in artificial soil, DACO: 9.3.2.2
3349396	2016, BCS-CS55621: Effects (Acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory - 1st final report amendment, DACO: 9.2.4.2
3349655	2019, BCS-CS55621 SC 20 G: Effects (acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory, DACO: 9.2.4.1,9.2.4.2
3349397	2019, BCS-CS55621-pyrazole acetic acid (BCS-CC26101): Effects (Acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory, DACO: 9.2.4.2
3349399	2019, BCS-CS55621-pyrazole alanine (BCS-DE61185): Effects (Acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory, DACO: 9.2.4.2

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3349401	2019, BCS-CS55621-pyrazole-methylsulfinyl acid (BCS-DE72760): Effects (acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory, DACO: 9.2.4.2
3349403	2019, BCS-CS55621-pyrazole-alanine-oxopropanoic acid (BCS-DE72761): Effects (acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory, DACO: 9.2.4.2
3349407	2016, BCS-CS55621 - Honey bee (*Apis mellifera* L.) larval toxicity test (repeated exposure) - Final report, DACO: 9.2.4.3
3349408	2018, BCS-CS55621 Al - Repeated exposure to honey bee (*Apis mellifera*) larvae under laboratory conditions (in vitro), DACO: 9.2.4.3
3349410	2018, Chronic toxicity of BCS-CS55621 AI to the honey bee *Apis mellifera* L. under laboratory conditions, DACO: 9.2.4.4
3349662	2019, BCS-CS55621 SC 20 (20 g/L): Chronic toxicity to the honey bee *Apis mellifera* L. under laboratory conditions, DACO: 9.2.4.4
3349660	2019, BCS-CS55621 SC 20 (20 g/L) - Repeated exposure to honey bee larvae (*Apis mellifera* L.) under laboratory conditions, DACO: 9.2.4.3
3349405	2018, BCS-CS55621 tech.: Effects (acute contact and oral) on bumble bees (*Bombus terrestris* L.) in the laboratory - Final report - DACO: 9.2.4.9
3349657	2019, BCS-CS55621 SC 20 (20 g/L): Effects (Acute contact and oral) on bumblebees (*Bombus terrestris* L.) in the laboratory, DACO: 9.2.4.1,9.2.4.2
3349664	2019, 1st final report amendment - BCS-CS55621 SC 20 (20 g/L): Toxicity testing on honey bees (*Apis mellifera* L.) under semi-field conditions in Germany - Tunnel test, DACO: 9.2.4.6
3349666	2022, BCS-CS55621 SC 20 (20 g/L): Toxicity testing on honey bees (*Apis mellifera* L.) under semi-field conditions in Spain - Tunnel test, DACO: 9.2.4.6
3349667	2019, Toxicity to the predatory mite *Typhlodromus pyri* (*Acari: Phytoseiidae*) using a laboratory test; fluoxapiprolin SC 20 g/L, DACO: 9.2.5
3349668	2019, Toxicity to the parasitoid wasp *Aphidius rhopalosiphi* (*Hymenoptera: Braconidae*) using a laboratory test; fluoxapiprolin SC 20 g/L, DACO: 9.2.6
3349670	2019, BCS-CS55621 SC 20 G: Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.7
3349411	2019, BCS-CS55621-BDM-pyrazole (BCS-BP32808): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5
3349412	2019, BCS-CS55621-piperidine (HCl salt) (BCS-CU97237): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5
3349413	2019, Amendment no. 01: BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5

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3349414	2019, BCS-CS55621-pyrazole-acetic acid (BCS-CC26101): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5
3349415	2019, BCS-CS55621-thiazole acid (sodium salt) (BCS-DH17585): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5
3349416	2019, BCS-CS55621-lactam (BCS-DA63612): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5
3349417	2019, BCS-CS55621-4-OH piperidine (BCS-CY96288): Influence on mortality and reproduction of the soil mite species *Hypoaspis aculeifer* tested in artificial soil, DACO: 9.2.5
3349669	2019, BCS-CS55621 SC 20 (20 g/L): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349438	2019, BCS-CS55621-BDM-pyrazole (BCS-BP32808): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349439	2019, BCS-CS55621-piperidine (HCl salt) (BCS-CU97237): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349441	2019, BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349442	2019, BCS-CS55621-pyrazole-acetic acid (BCS-CC26101): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349443	2019, BCS-CS55621-thiazole acid (sodium-salt) (BCS-DH17585): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349444	2019, BCS-CS55621-4-OH piperidine (BCS-CY96288): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349445	2019, BCS-CS55621-lactam (BCS-DA63612): Influence on mortality and reproduction of the collembolan species *Folsomia candida* tested in artificial soil, DACO: 9.2.7
3349528	2018, Amendment no. 01 - Acute toxicity of BCS-CS55621 (tech.) to the waterflea *Daphnia magna* in a static laboratory test system, DACO: 9.3.2
3349671	2019, Acute toxicity of BCS-CS55621 SC 20 G to the waterflea *Daphnia magna* in a static laboratory test system, DACO: 9.3.2
3349419	2018, Daphnia sp., acute immobilisation test with BCS-CS55621-BCS-BP32808, DACO: 9.3.2

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3349420	2019, BCS-CS55621-pyrazole acetic acid (BCS-CC26101) - Acute toxicity to *Daphnia magna* in a semi-static 48-hour immobilisation limit test, DACO: 9.3.2
3349421	2019, BCS-CS55621-desmesyl (BCS-CS15122) - Acute toxicity to *Daphnia magna* in a static 48-hour immobilisation test, DACO: 9.3.2
3349422	2019, BCS-CS55621-lactam (BCS-DA63612): Acute toxicity to *Daphnia magna* in a static 48-hour immobilisation test, DACO: 9.3.2
3349423	2019, BCS-CS55621-piperidine (BCS-DC21250) tested as BCS-CS55621-piperidine (HCl salt; BCS-CU97237) - Acute toxicity to *Daphnia magna* in a static 48-hour immobilisation test - 1st final report amendment, DACO: 9.3.2
3349424	2019, BCS-CS55621-thiazole acid tested as BCS-DH17585 (Sodium salt): Acute toxicity to *Daphnia magna* in a static 48-hour immobilisation limit test, DACO: 9.3.2
3349425	2019, BCS-CS55621-4-OH piperidine (BCS-CY96288): Acute toxicity to *Daphnia magna* in a static 48-hour immobilisation test, DACO: 9.3.2
3349426	2019, BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260) Acute toxicity to *Daphnia magna* in a static 48-hour immobilisation limit test, DACO: 9.3.2
3349427	2019, BCS-CS55621 - Influence to *Daphnia magna* in a semi-static reproduction test - 2nd final report amendment, DACO: 9.3.3
3349430	2019, BCS-CS55621 - Acute toxicity test with mysids (*Americamysis bahia*) under static conditions, DACO: 9.4.2
3349431	2022, BCS-CS55621 - Acute toxicity test to Eastern oyster (*Crassostrea virginica*) , DACO: 9.4.4
3349542	2021, BCS-CS55621 - Life-cycle toxicity test with mysids (*Americamysis bahia*), DACO: 9.4.5
3349433	2021, Fluoxapiprolin: Amphibian metamorphosis assay for the detection of thyroid active substances using a time-to-stage design, DACO: 9.9
3349434	2021, Fluoxapiprolin: Fish short-term reproduction assay with the fathead minnow (*Pimephales promelas*) - Final report, DACO: 9.9
3349459	2020, Amendment no. 02:- BCS-CS55621: A life cycle toxicity test with the midge (*Chironomus dilutus*) using spiked sediment, DACO: 9.3.4
3349447	2018, Acute toxicity of BCS-CS55621 (tech.) to larvae of *Chironomus riparius* in a 48 h static laboratory test system, DACO: 9.3.4
3349462	2020, *Chironomus riparius* 28-day chronic toxicity test with BCS-CS55621 tech. in a water-sediment system using spiked water, DACO: 9.3.4
3349463	2019, *Chironomus riparius* 28-day chronic toxicity test with BCS-CS55621 tech. in a water-sediment system using spiked sediment, DACO: 9.3.4
3349460	2020, Amended final report - BCS-CS55621: A life cycle toxicity test with the freshwater amphipod (*Hyalella azteca*) using spiked sediment, DACO: 9.3.4
3349451	2020, Amended final report - BCS-CS55621: A life cycle toxicity test with the marine amphipod (*Leptocheirus plumulosus*) using spiked sediment, DACO: 9.4.5

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3349470	2019, Amendment no. 1 to BCS-CS55621 tech. - Acute toxicity to rainbow trout (*Oncorhynchus mykiss*) under static conditions, DACO: 9.5.2.1
3349471	2019, BCS-CS55621 - Acute toxicity test with fathead minnow (*Pimephales promelas*) under static conditions, DACO: 9.5.2.1
3349472	2021, BCS-CS55621 - Acute toxicity test with sheepshead minnow (*Cyprinodon variegatus*) under static conditions, DACO: 9.5.2.4
3349475	2019, BCS-CS55621 - Early life-stage toxicity test with fathead minnow (*Pimephales promelas*), DACO: 9.5.3.1
3646953	2024, BCS-CS55621: An Early Life-Stage Toxicity Test with the Sheepshead Minnow (*Cyprinodon variegatus*), DACO: 9.5.3.1
3349482	2020, [pyrazole-4-^{14}C]BCS-CS55621- Aqueous exposure bioconcentration fish test and biotransformation in fish (*Lepomis macrochirus*), DACO: 9.5.6
3349483	2016, Acute oral LIMIT-test toxicity of BCS-CS55621 (techn.) to bobwhite quail (*Colinus virginianus*), DACO: 9.6.2.1
3349673	2020, Fluoxapiprolin SC 20: Acute oral toxicity test with northern bobwhite (*Colinus virginianus*), DACO: 9.6.4
3349484	2017, Amendment no. 2 - Toxicity of BCS-CS55621 technical during an acute oral LD_{50} with the canary (*Serinus canaria*), DACO: 9.6.2.3
3349485	2017, Amendment no. 3 - Toxicity of BCS-CS55621 technical during a dietary LC_{50} with the Northern bobwhite quail (*Colinus virginianus*), DACO: 9.6.2.4
3349486	2017, Amendment no. 3 - Toxicity of BCS-CS55621 technical during a dietary LC_{50} with the mallard duck (*Anas platyrhynchos*), DACO: 9.6.2.5
3349487	2018, Amendment no. 03: Toxicity of BCS-CS55621 technical in the reproduction of the northern bobwhite quail (*Colinus virginianus*), DACO: 9.6.3.1
3349489	2019, BCS-CS55621: A reproduction study with the mallard, DACO: 9.6.3.2
3349490	2019, BCS-CS55621 - 96-hour toxicity test with the freshwater diatom, *Navicula pelliculosa*, DACO: 9.8.2
3349492	2019, *Pseudokirchneriella subcapitata* growth inhibition test with BCS-CS55621 (tech.), DACO: 9.8.2
3349494	2019, BCS-CS55621-BDM-pyrazole (BCS-BP32808): Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2
3349495	2019, BCS-CS55621-pyrazole acetic acid (BCS-CC26101) - Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2
3349505	2019, BCS-CS55621-desmesyl (BCS-CS15122) - Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2
3349508	2019, BCS-CS55621-lactam (BCS-DA63612): Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2

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3349509	2019, BCS-CS55621-piperidine (BCS-DC21250) tested as BCS-CS55621-piperidine (HCl salt; BCS-CU97237) - Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test - 1st final report amendment, DACO: 9.8.2
3349510	2019, BCS-CS55621-thiazole acid tested as BCS-DH17585 (Sodium salt): Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2
3349512	2019, BCS-CS55621-pyrazole-carboxylic acid (BCS-CZ38260): Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2
3349514	2019, BCS-CS55621 - 96-hour toxicity test with the freshwater cyanobacterium, *Anabaena flos-aquae*, DACO: 9.8.2,9.8.6
3349515	2019, BCS-CS55621-4-OH piperidine (BCS-CY96288): Toxicity to *Pseudokirchneriella subcapitata* in an algal growth inhibition test, DACO: 9.8.2
3349516	2019, BCS-CS55621 - 96-hour toxicity test with the marine diatom, *Skeletonema costatum*, DACO: 9.8.3
3349518	2018, *Lemna gibba* G3 - Growth inhibition test with BCS-CS55621 under static conditions - Final report, DACO: 9.8.5
3349672	2019, BCS-CS55621 SC 20 G - Acute toxicity to rainbow trout (*Oncorhynchus mykiss*) under static conditions, DACO: 9.5.2.1,9.5.2.2
3349677	2019, *Pseudokirchneriella subcapitata* growth inhibition test with BCS-CS55621 SC 20 G - Final report -, DACO: 9.8.2
3349679	2019, Amendment no. 1 to effects on the seedling emergence and growth of ten species of non-target terrestrial plants (Tier 1) fluoxapiprolin SC 20 (20 g/L), DACO: 9.8.4
3349680	2019, Amendment no. 2 to effects on the vegetative vigor of ten species of non-target terrestrial plants (Tier 1) - Fluoxapiprolin SC 20 (20 g/L), DACO: 9.8.4
3349681	2021, Effects on the seedling emergence and growth of *Brassica napus* (Tier 2); fluoxapiprolin SC 20 (20 g/L) - Amendment no. 1 to final report DART-M-782712-01-1, DACO: 9.8.4
3349682	2019, *Lemna gibba* G3 - Growth inhibition test with BCS-CS55621 SC 20 G under static conditions, DACO: 9.8.5

4.0 Value

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3349698	2022, Value Document, DACO: 10.1,10.2,10.2.1,10.2.2,10.2.3.3,10.2.3.3(B),10.2.4, 10.3,10.3.1,10.3.2,10.3.2(A),10.3.3,10.4,10.5,10.5.1,10.5.2,10.5.3

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3349699	2022, Field Trial Reports, DACO: 10.2.3.4(B),10.3.2(A)
3421231	2022, Rationale justifying extrapolating the claim of suppression of phytophthora blight caused by *Phytophthora capsici* on fruiting vegetables (crop group 8-09), DACO: 10.2
3349578	2022, A benefits document supporting the registration of fluoxapiprolin to control economically important and difficult-to-control oomycete diseases on brassica vegetables, bulb vegetables, cucurbit vegetables, fruiting vegetables, grapes, leaf petiole vegetables, leafy vegetables, and potatoes, DACO: 10.6