Proposed Registration Decision PRD2016-11

Fluopyram

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Table of Contents

Overview

Proposed Registration Decision for Fluopyram

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Fluopyram Technical Fungicide and three end-use products, FLU+TFS 1 :1 SC Fungicide containing the technical grade active ingredients fluopyram and trifloxystrobin, and Fluopyram ST and Fluopyram Greenhouse Fungicide, both containing the technical grade active ingredient fluopyram. All three end-use products are used to control several fungal diseases on turfgrass, soybean seeds or food crops.

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

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Fluopyram Technical Fungicide, FLU+TFS 1:1 SC Fungicide, Fluopyram ST, and Fluopyram Greenhouse Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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

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

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

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

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

What Is Fluopyram?

Fluopyram is a conventional active ingredient with fungicidal properties. It acts on pathogen cells by inhibiting their normal respiration process. Fungicide products containing fluopyram are applied as foliar spray, drip irrigation or drench, and seed treatment on various greenhouse crops, turfgrass and soybeans to manage economically important plant diseases.

Health Considerations

Can Approved Uses of Fluopyram Affect Human Health?

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

Potential exposure to fluopyram may occur through the diet (food and water), when handling and applying the products or when entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when pesticide products are used according to label directions.

[3] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.
[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

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

The acute toxicity of the end-use product FLU+TFS 1:1 SC Fungicide was low via the oral, dermal and inhalation routes of exposure. The product was minimally irritating to the eyes and skin. It caused allergic skin reactions; consequently, the hazard statement "POTENTIAL SKIN SENSITIZER" is required on the label.

The acute toxicity of the end-use product Fluopyram ST was slight via the oral route of exposure and low via the dermal and inhalation routes of exposure. It was non-irritating to the eyes and skin and did not cause an allergic skin reaction. The hazard statement "CAUTION – POISON" is required on the label.

The acute toxicity of the end-use product Fluopyram Greenhouse Fungicide was low via the oral, dermal and inhalation routes of exposure. The product was minimally irritating to the eyes and non-irritating to the skin. It did not cause an allergic skin reaction.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests were assessed for the potential of fluopyram to cause neurotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, genetic damage and various other effects. The most sensitive endpoints used for risk assessment were decreased activity and effects on the liver, thyroid and kidneys. There were no indications that the young were more sensitive to fluopyram than the adult animal. Fluopyram caused liver tumours in rats and thyroid tumours in mice. These tumours were observed at high dose levels.

The risk assessment protects against these and any other potential effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Risks in Residential and Other Non-Occupational Environments

Residential and non-occupational risks are not of concern when FLU+TFS 1:1 SC Fungicide is used according to the label directions.

Adults, youth and children may be exposed to fluopyram while golfing on courses treated with FLU+TFS 1:1 SC Fungicide. Based on the expected short-term duration of this activity, risk to children, youth and adults is not a concern.

Occupational Risks from Handling Fluopyram Greenhouse Fungicide, Fluopyram ST and FLU+TFS 1:1 SC Fungicide

Occupational risks are not of concern when the products containing fluopyram are used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply fluopyram, as well as workers re-entering freshly treated greenhouses and turf or treating seeds can come in direct contact with fluopyram residues on the skin. Therefore, the labels specify that anyone mixing/loading and applying Fluopyram Greenhouse Fungicide and FLU+TFS 1:1 SC Fungicide must wear a long-sleeved shirt, long pants, shoes plus socks, and chemical-resistant gloves. In addition, the Fluopyram ST label specifies that treaters must wear a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes and socks. When cleaning seed treatment equipment, workers must wear coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes and socks. Workers bagging, sewing, stacking or fork lifting treated seed must wear a long-sleeved shirt, long pants, and shoes and socks; gloves are recommended for good hygiene practices. Anyone involved with the handling of treated seeds (including planting) must also wear a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes and socks. Workers planting more than 2900 kg of treated soybean seeds must also use closed-cab tractors. The Fluopyram Greenhouse Fungicide label also requires that workers do not enter treated greenhouses for 12 hours after application. The FLU+TFS 1:1 SC Fungicide requires that workers do not enter sod farms for 12 hours after application and golf courses until sprays have dried. Taking into consideration these label statements, the number of applications and the anticipated exposure period for handlers and workers, health risks to these individuals are not a concern. Furthermore, the endpoints selected for worker risk assessment are also protective of any potential cancer findings and there are no health risks of concern.

FLU+TFS 1:1 SC Fungicide is a co-formulation with trifloxystrobin. Trifloxystrobin is registered for use on sod farms and golf courses. The precautions required to mitigate risk from the exposure of fluopyram are also adequate for the co-formulated active ingredient.

For bystanders, exposure is expected to be much less than that for workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Residues in Water and Food

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

Aggregate chronic (cancer and non-cancer) dietary intake estimates (food plus water) revealed that the general population and children 1-2 years old, the subpopulation which would ingest the most fluopyram relative to body weight, are expected to be exposed to less than 98% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluopyram is not of health concern for all population subgroups. The lifetime cancer risk from the use of fluopyram is not of health concern.

Aggregate acute dietary intake estimates (food and water) for the general population and all population subgroups were less than 38% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was children 1-2 years old.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout the United States, including Canadian representative growing regions, using fluopyram on soybeans, and in greenhouses in Europe using fluopyram on tomatoes, peppers, cucumbers and lettuce are acceptable. The MRLs for this active ingredient in/on dry soybeans, tomatoes and cucumbers can be found in the Science Evaluation section of this Consultation Document. MRLs to cover residues of fluopyram in/on lettuce and peppers are under promulgation, based on crop grouping principles and residue data generated following foliar field applications. The use of fluopyram in greenhouses on these crops is not expected to result in residues exceeding these MRLs.

Environmental Considerations

What Happens When Fluopyram Is Introduced Into the Environment?

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

Fluopyram can enter the environment when it is applied as a fungicide on turf and seed. Fluopyram does not breakdown readily in soils and therefore has the potential for residue carry over to the following crop season. It is moderately mobile in soils and has a potential to move downward through the soil and enter groundwater. Fluopyram is unlikely to enter the atmosphere and be transported to areas far removed from where it was applied. Fluopyram is not expected to accumulate in the tissues of organisms.

When used according to the label directions, fluopyram does not present risks of concern to birds, small mammals, fish, algae, earthworms, bees, invertebrates and aquatic plants. The use of the end-use product, Fluopyram ST may pose a risk to small mammals and birds. The use of the end-use product, FLU+TFS 1:1 SC Fungicide, may pose a risk to non-target terrestrial plants and amphibians. The use of the end-use product Fluopyram Greenhouse Fungicide is not anticipated to present an unacceptable risk to non-target terrestrial and non-target aquatic organisms. Spray buffer zones are specified on the product label of FLU+TFS 1:1 SC Fungicide to protect terrestrial and freshwater habitats adjacent to treated areas and specific instructions are provided to prevent runoff into aquatic habitats. Precaution statements are also specified on the product label to inform users that fluopyram can be toxic to terrestrial plants and amphibians. Precaution statements and seed labeling requirements are specified on the product label of Fluopyram ST to inform users that fluopyram can be toxic to small mammals and birds.

Value Considerations

What Is The Value of FLU+TFS 1:1 SC Fungicide, Fluopyram ST, and Fluopyram Greenhouse Fungicide?

Fluopyram and tryfloxystrobin, the active ingredients in FLU+TFS 1:1 SC Fungicide, control important summer diseases on turfgrass.
FLU + TFS 1:1 SC Fungicide controls dollar spot, brown patch and leaf spot on turfgrass. The addition of the active ingredient, fluopyram with trifloxystrobin, will offer an additional chemistry to control dollar spot on turfgrass and help manage resistance development since the dollar spot pathogen has developed resistance to other commonly used active ingredients.

Fluopyram, the active ingredient in Fluopyram ST, controls sudden death syndrome in soybean.
Currently, very few fungicide products are registered to control sudden death syndrome (SDS) of soybean in Canada. SDS was first identified in Ontario in 1998. Since then, it has become a prominent and economically important disease in southwestern Ontario. In some areas, SDS now ranks among the top-tier of yield-reducing diseases of soybean.

Fluopyram, the active ingredient in Fluopyram Greenhouse Fungicide, also controls prevalent diseases, including grey mould, powdery mildew, and blights in major greenhouse crops.
In addition to providing Canadian greenhouse vegetable producers with a new and effective option for the management of major diseases in tomato, cucumbers, peppers, and lettuce, registration of this product also offers a new method of application for this group of fungicides with either drip or drench treatments to control botrytis in tomato. This application method is particularly suitable to greenhouse vegetable production in Canada given the common use of hydroponic technologies and drip irrigation in most commercial operations.

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 FLU+TFS 1 :1 SC Fungicide, Fluopyram ST, and Fluopyram Greenhouse Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with fluopyram residues on the skin or through inhalation of spray mist, anyone mixing, loading and applying Fluopyram Greenhouse Fungicide and FLU+TFS 1:1 SC Fungicide must wear a long-sleeved shirt, long

pants, shoes plus socks, and chemical resistant gloves. In addition, the Fluopyram ST label specifies that treaters must wear a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes and socks. When cleaning seed treatment equipment, workers must wear coveralls over a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes and socks. Workers bagging, sewing, stacking or fork lifting treated seed must wear a long-sleeved shirt, long pants, and shoes and socks; gloves are recommended for good hygiene practices. Anyone involved with the handling of treated seeds (including planting) must also wear a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes and socks. Workers planting more than 2900 kg of treated soybean seeds must also use closed-cab tractors.

The Fluopyram Greenhouse Fungicide label also requires that workers do not enter treated greenhouses for 12 hours after application. The FLU+TFS 1:1 SC Fungicide requires that workers do not enter sod farms for 12 hours after application and golf courses until sprays have dried.

Environment

To minimize potential risks to non-target terrestrial plants, small mammals, birds and amphibians, label statements, seed labeling statements and no-spray buffer zones to protect sensitive terrestrial and aquatic habitats are specified on the end-use product labels for Fluopyram ST and FLU+TFS 1:1 SC Fungicide.

Next Steps

Before making a final registration decision on fluopyram, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document.

Other Information

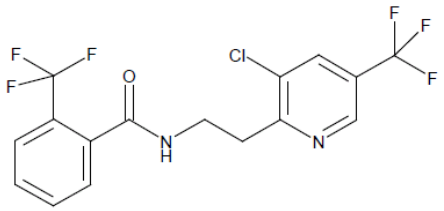
When the PMRA makes its registration decision, it will publish a Registration Decision on fluopyram (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA’s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

Science Evaluation

Fluopyram

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Fluopyram
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	*N*-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]ethyl}-2-(trifluoromethyl)benzamide
2. Chemical Abstracts Service (CAS)	*N*-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)- benzamide
CAS number	658066-35-4
Molecular formula	$C_{16}H_{11}ClF_6N_2O$
Molecular weight	396.72
Structural formula	
Purity of the active ingredient	97.4%

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

Technical Product—Fluopyram Technical Fungicide

Property	Result
Colour and physical state	White solid
Odour	No noticeable odour
Melting range	118.0°C
Boiling point or range	319 °C (under decomposition)
Density	1.53 g/cm^3

Property	Result
Vapour pressure at 20°C	1.2×10^{-6} Pa
Henry's law constant at 20°C	2.98×10^{-5} Pa×m^3×mol^{-1}
Ultraviolet (UV)-visible spectrum	λ_{max} = 270 nm
Solubility in water at 20°C	16 mg/L
Solubility in organic solvents at 20°C	Solvent — Solubility (g/L) acetone > 250 dichloroethane > 250 dimethyl sulfoxide > 250 ethyl acetate > 250 n-heptane 0.66 methanol > 250 toluene 62.2
n-Octanol-water partition coefficient (K_{ow})	Log K_{ow} = 3.3 at 20°C
Dissociation constant (pK_a)	No pKa value could be detected in the range of 2 < pH < 12
Stability (temperature, metal)	The test item showed an endothermic effect (melting) in the temperature range 105–130°C and an exothermal decomposition in the temperature range 310–400°C with an energy of 285 J/g.

End-Use Products

Property	FLU+TFS 1:1 SC Fungicide	Fluopyram ST	Fluopyram Greenhouse Fungicide
Colour	Green or Colourless	Off-white	Beige
Odour	Slight pungent odour	Slightly musty odour	Chemical odour
Physical state	Liquid	Liquid	Liquid
Formulation type	Suspension	Suspension	Suspension
Guarantee	Fluopyram 12.5 g/L Trifloxystrobin 12.5 g/L	Fluopyram 600 g/L	Fluopyram 500 g/L
Container material and description	Plastic 1 L to bulk	Plastic 0.2 to 1000 L	Plastic 0.5 L to bulk
Density/Specific gravity	1.03–1.07 g/mL	1.22–1.26	1.205 g/mL
pH of 5% dispersion in water	5.0–7.0	7.8	6.5
Oxidizing or reducing action	Does not contain any oxidising or reducing agent.	Does not contain any oxidising or reducing agent.	Does not contain any oxidising or reducing agent.

Property	FLU+TFS 1:1 SC Fungicide	Fluopyram ST	Fluopyram Greenhouse Fungicide
Storage stability	Stable when stored for two weeks at 54°C in commercial packaging.	Stable when stored for two weeks at 54°C in commercial packaging.	Stable over 12 months in HDPE packaging at ambient temperature.
Corrosion characteristics	Not corrosive to the packaging material.	Not corrosive to the packaging material when stored for 8 weeks at 40°C.	Not corrosive to the container material
Explodability	Not considered to be potentially explosive.	Not considered to be potentially explosive.	Not considered to be potentially explosive.

1.3 Directions for Use

Fungicide products containing fluopyram are applied by foliar spray, drip irrigation or drench, and seed treatment on various greenhouse crops, turfgrass and soybeans to manage economically important plant diseases. FLU + TFS 1:1 SC Fungicide is applied in a foliar spray to turfgrass at a rate of 140 to 200 ml/100m^2 with a reapplication interval of 14 to 28 days. Fluopyram ST is applied to the soybean seeds at a rate of 0.15 to 0.25 mg active ingredient/seed. Fluopyram Greenhouse Fungicide is applied as a foliar spray to greenhouse cucumber, pepper, tomato, and lettuce at a rate range of 100-500 mL/ha with a seven to ten day reapplication intervals. Fluopyram Greenhouse Fungicide can also be applied as a drip or drench application to greenhouse tomatoes at a rate of 40 mL per 1000 plants with a maximum single application rate of 500 mL/ha.

1.4 Mode of Action

Please refer to ERC2014-02, *Fluopyram* and PRD2016-05, *Fluopyram.*

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

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

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

Please refer to ERC2014-02, *Fluopyram* and PRD2016-05, *Fluopyram*, for the residue analytical methods in plant and animal matrices for data generation and enforcement purposes.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for fluopyram was conducted previously and is summarized in PRD2016-05, *Fluopyram* and Evaluation Report ERC2014-02, *Fluopyram*.

The acute toxicity of the end-use product FLU+TFS 1:1 SC Fungicide was low via the oral, dermal and inhalation routes in rats. It was minimally irritating to the eyes and skin of rabbits. It was a dermal sensitizer in mice by the LLNA method.

The acute toxicity of the end-use product Fluopyram ST was slight via the oral route and low via the dermal and inhalation routes in rats. It was non-irritating to the eyes and skin of rabbits and was not a dermal sensitizer in mice by the LLNA method.

The acute toxicity of the end-use product Fluopyram Greenhouse Fungicide was low via the oral, dermal and inhalation routes in rats. It was minimally irritating to the eyes and non-irritating to the skin of rabbits. It was not a dermal sensitizer in mice by the LLNA method. Please see Appendix I, Table 3, for details.

Cancer Assessment

The cancer assessment was revised based on data received under a previous application. The results of those revisions were published in PRD2016-05, *Fluopyram*.

Incident Reports

Since April 26, 2007, registrants have been required by law to report pesticide incidents to the PMRA that are related to their products. In addition, the general public, medical community, government and non-governmental organizations are able to report pesticide incidents directly to the PMRA. As of November 30, 2015, no human or domestic animal incident reports involving fluopyram have been submitted to the PMRA.

Toxicological Endpoints

Please see Appendix I, Table 4, for details. Also, refer to PRD2016-05, *Fluopyram* and ERC2014-02, *Fluopyram* for a summary of the previously reviewed data.

3.1.1 *Pest Control Products Act* Hazard Characterization

Please refer to ERC2014-02, *Fluopyram* for a summary of the previously reviewed data.

3.2 Determination of Acute Reference Dose

Please refer to ERC2014-02, *Fluopyram* for a summary of the previously reviewed data.

3.3 Determination of Acceptable Daily Intake

Please refer to ERC2014-02, *Fluopyram* for a summary of the previously reviewed data.

3.4 Occupational and Residential Risk Assessment

3.4.1 Dermal Absorption

Please refer to ERC2014-02, *Fluopyram* for a summary of the previously reviewed data.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Greenhouse Uses of Fluopyram

Fluopyram Greenhouse Fungicide can be applied on greenhouse cucumbers, peppers, tomatoes and lettuce.

3.4.2.1.1 Greenhouse Mixer/loader/applicator Exposure and Risk Assessment

Exposure to workers who mix/load and apply Fluopyram Greenhouse Fungicide on greenhouse vegetables is expected to last for up to 180 days per year (short- to intermediate-term exposure duration). Individuals have potential for dermal and inhalation exposure to Fluopyram Greenhouse Fungicide during mixing, loading and application. As such, a quantitative dermal and inhalation risk assessment is required. Exposure estimates were derived for mixers/loaders/applicators applying Fluopyram Greenhouse Fungicide to greenhouse cucumbers, tomatoes, lettuce and peppers using chemigation, backpack, manually-pressurized handwand and mechanically-pressurized handgun. The exposure estimates are based on mixers/loaders/applicators wearing a single layer of clothing plus chemical-resistant gloves for all application methods.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. A dermal absorption value was not required in the calculation of dermal exposure, since the short- to intermediate-term dermal endpoint is based on a dermal toxicity study. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day and 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 80 kg adult body weight.

Exposure estimates were compared to the toxicological endpoints (NOAEL: no observed adverse effects level) to obtain the margin of exposures (MOEs) in Table 3.4.2.1.1; the target MOE is 100 for both dermal and inhalation exposure. No health risks of concern were identified when workers followed the recommended precautions on the label.

Table 3.4.2.1.1: Mixer/Loader/Applicator Dermal and Inhalation Exposure Estimates and MOEs

Exposure scenario	PHED unit exposure (µg/kg a.i.)[1]		Maximum application rate (kg a.i./ha)	Volume handled per day (litres)[2]	Exposure (mg/kg bw/day)		Calculated MOE[5]	
	Dermal	Inhalation			Dermal[3]	Inhalation[4]	Dermal	Inhalation
Manually-Pressurized Handwand	943.37	45.20	0.250	150	8.84E-04	4.24E-05	339,000	29,500
Backpack	5443.85	62.10	0.250	150	5.11E-03	5.82E-05	58,800	21,500
Mechanically-Pressurized Handgun	5585.49	151.00	0.250	3800	1.33E-01	3.59E-03	2260	3490
Chemigation in greenhouses	51.14	1.60	0.250	3 (ha/day)	9.79E-04	1.50E-05	62,600	83,300

[1] Exposure was estimated for workers wearing a single layer plus gloves.
[2] Default volume handled per day values; 3 ha/day for chemigation based on the 95th percentile of greenhouse size in Canada (2011 census)
[3] Dermal exposure = (PHED unit-exposure x rate x spray (volume/day /500L/ha dilution rate) x 0.001 kg/g x 0.001 mg/µg) / 80 kg bw)
[4] Inhalation exposure = (PHED unit-exposure x rate x spray (volume/day /500L/ha dilution rate) x 0.001 kg/g x 0.001 mg/µg x 100% inhalation absorption) / 80 kg bw)
[5] Margin of Exposure (MOE) = NOAEL $_{(route\text{-}specific)}$ / Exposure
Based on dermal NOAEL of 300 mg/kg bw/day, target MOE = 100
Based on inhalation NOAEL of 12.5 mg/kg bw/day, target MOE = 100

3.4.2.1.2 Exposure and Risk Assessment for Workers Entering Treated Greenhouses

There is potential for exposure to workers re-entering greenhouses treated with Fluopyram Greenhouse Fungicide to perform various activities including hand pruning, scouting, hand harvesting and irrigation. Given the nature of activities performed, dermal contact with treated surfaces is expected to occur throughout the season and exposure is expected to be long term as a result. A postapplication assessment was required.

Postapplication risk assessment was conducted using default dislodgeable foliar residue (DFR) values (25% dislodgeable at Day 0, 0% dissipation), Agricultural Reentry Task Force (ARTF) transfer coefficients for greenhouse vegetables, and the dermal absorption value of 7%. Exposure estimates were compared to the long-term dermal toxicological endpoint (NOAEL = 1.2 mg/kg bw/day) to obtain the MOEs in Table 3.4.2.1.2; the target MOE is 100. No health risks of

concern were identified when workers followed the recommended restricted entry interval (REI) on the label.

Table 3.4.2.1.2: Exposure and Risk Assessment for Workers Entering Treated Greenhouses

Re-entry activity	Peak DFR ($\mu g/cm^2$)[1]	Transfer coefficient (cm^2/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	Calculated MOE[4]	REI[5]
Cucumber, pepper, tomato, all activities	1.25	1400	1.22E-02	98	12 hrs
Lettuce, all activities	1.25	230	2.01E-03	600	12 hrs

[1] Calculated using the default 25% dislodgeable on the day of application and 0% dissipation per day
[2] Transfer coefficients (TC) obtained from ARTF TC database
[3] Exposure = (Peak DFR [$\mu g/cm^2$] × TC [cm^2/hr] × 8 hours × 7% dermal absorption) / (80 kg bw × 1000 µg/mg)
[4] Based on a long-term NOAEL of 1.2 mg/kg bw/day, target MOE = 100
[5] Minimum REI is 12 hours to allow residues to dry

Inhalation exposure is not expected to occur since workers and bystanders are not allowed to enter until 12 hours after application and the vapour pressure of fluopyram is estimated to be 1.2×10^{-6} Pa (20°C). This vapour pressure is less than the NAFTA waiver for an inhalation study of $<1 \times 10^{-5}$ kPa (7.5×10^{-5} mmHg) for indoor uses.

3.4.2.2 Seed Treatment Uses of Fluopyram

Fluopyram ST can be used for commercial seed treatment (in facilities or with mobile treaters) of soybean seeds.

3.4.2.2.1 Commercial Seed Treatment Exposure and Risk Assessment

Individuals have potential for exposure to Fluopyram ST during the commercial seed treatment of soybean seed. Exposure to workers is expected to be short- to intermediate-term in duration and to occur primarily by the dermal and inhalation routes.

Chemical-specific data for assessing exposure during commercial seed treatment were not submitted. As such, a previously reviewed surrogate exposure study was used to estimate risk to workers involved in commercial seed treatment.

In the surrogate study, worker exposure to three active ingredients was monitored in commercial seed treatment facilities treating canola seed and corn seed. The two facilities treating canola seed were in Canada with workers wearing clothing representing coveralls over a single layer and chemical-resistant gloves. The three facilities treating corn seed were in the United States with workers wearing clothing representing a single layer, as well as chemical-resistant gloves when treating and cleaning out equipment. A total of twenty four male workers were monitored during the study. Dermal exposure was estimated by measuring residues on or in inner whole body dosimeters, face/neck wipes, and hand washes. Inhalation exposure was estimated by measuring residues in an Occupational Safety & Health Administration (OSHA) Versatile Sampler (OVS) tube fitted to a personal air sampling pump. Three different job activities were monitored at the sites: 1) treatment of seed, including mixing, loading and operation of the seed treatment equipment; 2) packaging of treated seeds, including bagging, sewing, stacking and

forklift operations; and 3) cleaning of seed treatment and seed handling equipment. The treatment solutions were prepared using closed transfer systems into the seed treatment equipment, except for five replicates in an American facility.

The dermal and inhalation exposure values are expressed as µg/kg ai handled for treaters and bagger/sewer/stackers. The dermal exposure of equipment cleanout operators is provided in µg/g ai/100 kg seed (i.e. normalized by application rate). As it is not possible to determine the amount of active ingredient handled per day for cleaners, exposure to these workers was normalized by the mean application rate used over the treatment period. Cleaners in the corn seed treatment facilities cleaned for less than 2 hours in total per day whereas the workers in facilities treating canola cleaned for an average of 8.35 hours. The monitoring duration of the cleaners in the corn seed treatment facilities is considerably shorter than a full work day. Since the typical duration of a work day for cleaners involved with soybean commercial seed treatment is uncertain, the cleaner exposure data from the canola seed treatment facilities was used to assess risk from use of Fluopyram ST. For the other worker types (treaters and bagger/sewer/stackers), exposure data from the corn seed treatment facilities was used. The arithmetic mean of exposure from all active ingredients was used for all activities since there were an adequate of replicates and the field recoveries were acceptable.

A seed treatment dust-off study was conducted on soybean seed treated with Fluopyram ST. The results were compared with previously reviewed dust-off data on canola and corn seed treated with other formulations that support the use of the surrogate study data. Results from the seed treatment dust level evaluation (dust-off) experiments indicated that the dust-off potential of soybean seed treated with tank-mixtures including Fluopyram ST (with colourant and polymer) is lower than canola and corn seed treated with the surrogate test materials. As such, based on the comparison of dust-off potentials, the surrogate study is not expected to underestimate exposure to workers involved with commercial seed treatment of soybean seed with Fluopyram ST.

Table 3.4.2.2.1 presents the risk estimates for the commercial seed treatment of soybean seed with Fluopyram ST. The calculated MOEs were above the target MOE of 100. No occupational risks of concern were identified from exposure to fluopyram when treating soybean seed in commercial seed treatment facilities. It is expected that the health risk to workers using commercial mobile equipment to treat seed would be similar to, or less than, the health risk to workers in commercial seed treatment facilities.

Table 3.4.2.2.1 Exposure and Risk Estimates for Workers in Commercial Seed Treatment Facilities Applying Fluopyram ST

Scenario	Unit Exposure (µg/kg ai handled)		kg ai handled per day[1]	Exposure [2] (mg/kg bw/day)		Calculated MOE [4]	
	Dermal	Inhalation		Dermal	Inhalation	Dermal	Inhalation
Treater/Applicator[2]	256	3.72	103.95	3.33E-01	4.83E-03	902	2590
Bagger/Sewer/ Stacker[2]	238	18.7	103.95	3.09E-01	2.43E-02	970	514
Cleanout Personnel [3]	56.2	12.7	165 g ai/100 kg seed	1.16E-01	2.62E-02	2590	477

[1] Kg ai handled per day = kg seed treated per day (63000 kg/day) × maximum application rate (0.00165 kg ai/kg seed)
The kg seed treated per day value for commercially treating soybean seed is from the AHETF survey
[2] For treater/applicators (single layer and chemical-resistant gloves) and bagger/sewer/stackers (single layer, no gloves), the corn subset from the surrogate study was used to calculate exposure:

$$\text{Exposure (mg/kg bw/day)} = \frac{\text{Unit exposure (µg/kg ai handled per day)} \times \text{kg ai handled per day}}{80 \text{ kg bw} \times 1000 \text{ µg/mg}}$$

[3] For cleanout personnel (coveralls over single layer and chemical-resistant gloves), the canola subset from the surrogate study was used to calculate exposure. Unit exposures are normalized for application rate; therefore:

$$\text{Exposure (mg/kg bw/day)} = \frac{\text{Unit exposure (µg ai/100 kg seed)} \times \text{application rate (g ai/100 kg seed)}}{80 \text{ kg bw} \times 1000 \text{ µg/mg}}$$

[4] Based on dermal NOAEL = 300 mg/kg bw/day, target MOE= 100; inhalation NOAEL = 12.5 mg/kg bw/day, target MOE = 100

3.4.2.2.2 Planting Exposure and Risk Assessment

There is potential for exposure to workers loading and planting soybean seed treated with Fluopyram ST. The duration of exposure is considered to be short-term, and the primary routes of exposure for workers handling treated seed would be via the dermal and inhalation routes.

Chemical-specific data for assessing planting exposure were not submitted. As such, surrogate exposure data have been used to estimate risk to workers involved in planting treated seed. In the previously reviewed surrogate passive dosimetry study, exposure was monitored for workers opening bags of treated corn seed, loading seed into the planter hopper, planting in closed-cab tractors, and cleaning and repairing planting equipment. Dermal exposure representing a single layer of clothing and chemical-resistant gloves was estimated by measuring residues on or in inner whole body dosimeters and outer work shirts (which were worn under a work jacket), face/neck wipes, and hand washes. Inhalation exposure was estimated by measuring residues in an Institute of Occupational Medicine (IOM) sampler fitted to a personal air sampling pump. Exposure values were normalized for the amount of active ingredient handled per day. The arithmetic mean was used for all activities as replicate numbers and field recoveries were acceptable.

No dust-off data were available for the products used in the surrogate planting exposure study. However, corn seed is expected to be dustier than soybean seed treated with tank-mixtures containing Fluopyram ST, based on the comparison of the dust-off data on Fluopyram ST-treated soybean seeds and previously reviewed dust-off data on corn seed. As such, the surrogate study is not expected to underestimate exposure from planting Fluopyram ST-treated soybean seed based on dust-off potential.

Table 3.4.2.2.2 presents the risk estimates for planting fluopyram-treated soybean seed. The calculated MOEs were above the target MOE of 100. No occupational risks of concern were identified from exposure to fluopyram when planting treated soybean seed when workers wear a single layer and chemical-resistant gloves. Closed-cab tractors are required for planting, since they were used in the surrogate exposure study. However, for workers handling 2900 kg of treated seeds or less, calculated MOEs were well above the target MOE of 100 and health risks are not of concern when open-cab tractors are used for planting.

Table 3.4.2.2.2 Exposure and Risk Estimates for Planting Fluopyram ST-Treated Seed

Scenario	Unit exposure (µg/kg ai handled)[1]		kg seed planted per day[2]	App rate (kg ai/kg seed)	kg ai handled per day[3]	Exposure[4] (mg/kg bw/day)		Calculated MOE[5]	
	Dermal	Inhalation				Dermal	Inhalation	Dermal	Inhalation
Planting	1515	82.83	9000	0.00165	15.85	2.81E-01	1.54E-02	1070	813
Planting	1515	82.83	2900	0.00165	4.785	9.06E-02	4.95E-03	3310	2520

[1] Exposure values for planters of treated soybean seed are from the surrogate planting exposure study
[2] The value 9000 kg/day is the default amount of soybean seed planted per day. The value 2900 kg/day is the amount of soybean seed planted per day that yields calculated MOEs well above the target MOE of 100.
[3] Kg ai handled per day = kg seed treated per day × application rate (kg ai/kg seed)
[4] Exposure (mg/kg bw/day) = $\frac{\text{Unit exposure (µg/kg ai handled per day)} \times \text{kg ai handled per day}}{80 \text{ kg bw} \times 1000 \text{ µg/mg}}$
[5] Based on a dermal NOAEL = 300 mg/kg bw/day and an inhalation NOAEL = 12.5 mg/kg bw/day; target MOE = 100

3.4.2.3 Turf Uses of Fluopyram

FLU+TFS 1:1 SC Fungicide can be applied on sod farms and golf courses.

3.4.2.3.1 Turf Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to fluopyram when mixing/loading and applying FLU+TFS 1:1 SC Fungicide on sod farms and golf courses. Exposure to workers is expected to be short- to intermediate-term in duration and to occur primarily by the dermal and inhalation routes.

Exposure estimates were derived for mixers/loaders/applicators applying FLU+TFS 1:1 SC Fungicide to commercial sod farms and golf courses using groundboom and turf gun. The exposure estimates were based on mixers/loaders/applicators wearing a single layer of clothing plus chemical-resistant gloves for all application methods. Dermal exposure was estimated by coupling the Pesticide Handlers Exposure Database (PHED), version 1.1 unit exposure values for sod farm workers and the Outdoor Residential Exposure Task Force (ORETF) for golf course workers with the amount of product handled per day, which is calculated by the maximum application rate and default area treated per day (ATPD) values for sod farms and golf courses. A dermal absorption value was not required in the calculation of dermal exposure, since the short- to intermediate-term dermal endpoint is based on a dermal toxicity study. Inhalation exposure

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

Exposure estimates were compared to the toxicological endpoints to obtain the MOEs in Table 3.4.2.3.1; the target MOE is 100 for both dermal and inhalation exposure. No health risks of concern were identified when workers followed the recommended precautions on the label.

Table 3.4.2.3.1: Mixer/Loader/Applicator Dermal and Inhalation Exposure Estimates and MOEs

Exposure scenario	PHED/ORETF unit exposure (µg/kg a.i.)[1]		ATPD (ha/day)[2]	Maximum application rate (kg a.i./ha)	Exposure (mg/kg bw/day)		Calculated MOE[5]	
	Dermal	Inhalation			Dermal[3]	Inhalation[4]	Dermal	Inhalation
Groundboom golf course	84.12	2.56	16	0.250	4.21E-04	1.28E-04	71,300	97,700
Groundboom sod farm	84.12	2.56	30	0.250	7.89E-04	2.40E-04	38,000	52,100
Turf gun	785	4.0	2	0.250	4.91E-03	2.50E-05	61,100	500,000

[1] Exposure was estimated for workers wearing a single layer plus gloves.
[2] Default area treated per day (ATPD) values
[3] Dermal exposure = (PHED unit-exposure x rate x ATPD x 0.001 kg/g x 0.001 mg/µg) / 80 kg bw
[4] Inhalation exposure = (PHED unit-exposure x rate x ATPD x 0.001 kg/g x 0.001 mg/µg x 100% inhalation absorption) / 80 kg bw
[5] Margin of Exposure (MOE) = NOAEL $_{(route\text{-}specific)}$ / Exposure
Based on dermal NOAEL of 300 mg/kg bw/day, target MOE = 100
Based on inhalation NOAEL of 12.5 mg/kg bw/day, target MOE = 100

3.4.2.3.2 Exposure and Risk Assessment for Workers Entering Treated Turf Areas

There is potential for exposure to workers re-entering sod farms and golf courses treated with FLU+TFS 1:1 SC Fungicide when performing various activities. The duration of exposure is expected to be short-term for all re-entry activities. The primary route of exposure for workers entering treated areas would be through the dermal route.

Postapplication risk assessment was conducted using default turf transferable residue (TTR) values (1% dislodgeable at Day 0, 10% dissipation per day) and Agricultural Reentry Task Force (ARTF) transfer coefficients. Exposure estimates were compared to the short-term dermal toxicological endpoint (NOAEL = 300 mg/kg bw/day) to obtain the MOEs in Table 3.4.2.3.2; the target MOE is 100. No health risks of concern were identified when workers followed the recommended restricted entry interval (REI) on the label.

Table 3.4.2.3.2: Exposure and Risk Assessment for Workers Entering Treated Turf Areas

Re-entry activity	Peak DFR/TTR (µg/cm^2)[1]	Transfer coefficient (cm^2/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	Calculated MOE[4]	REI
Postapplication Workers – Sod Farms and Golf Courses					
Transplanting/planting; slab harvesting (Golf course and/or sod farm)	0.0307	6700	2.06E-02	14,600	Golf courses: Until spray has dried Sod farms: 12 hours
Mowing, watering, cup changing, irrigation, repair, miscellaneous grooming (Golf course)	0.0307	3500	1.08E-02	27,900	
Aerating, fertilizing, hand pruning, mechanical weeding, scouting, seeding	0.0307	1000	3.07E-03	97,700	

[1] Calculated using the default for turf of 1% dislodgeable on the day of application and 10% dissipation per day
[2] Transfer coefficients obtained from ARTF TC database.
[3] Exposure = (Peak DFR/TTR [µg/cm^2] × TC [cm^2/hr] × Exposure Duration (8 hours for workers) / (80 kg bw × 1000 µg/mg)
[4] Based on NOAEL of 300 mg/kg bw/day, target MOE = 100

Inhalation exposure is not expected to occur since workers are not allowed to enter until 12 hours after application for sod farms, and since workers and golfers are not allowed to enter treated golf courses until residues have dried. Inhalation exposure is not considered to be a significant route of exposure for people entering treated areas compared to the dermal route, since fluopyram is relatively non-volatile (1.2×10^{-6} Pa at 20°C) and as such, an inhalation risk assessment was not required.

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

Fluopyram Greenhouse Fungicide, Fluopyram ST and FLU+TFS 1:1 SC Fungicide are not domestic products; therefore, a residential handler assessment was not required.

3.4.3.2 Postapplication Exposure and Risk

There is potential for recreational postapplication exposure from the use of FLU+TFS 1:1 SC Fungicide on golf courses. The duration of exposure is expected to be short-term for golfers and the primary route of exposure entering treated areas would be through the dermal route.

Postapplication risk assessment was conducted using default transferable turf residue (TTR) values (1% dislodgeable at Day 0, 10% dissipation per day). Exposure estimates were compared to the short-term dermal toxicological endpoint (NOAEL = 300 mg/kg bw/day) to obtain the MOE in Table 3.4.3.2; the target MOE is 100. No health risks of concern were identified when recreational users (golfers) followed the recommended REI on the label.

Table 3.4.3.2: Exposure and Risk Assessment for Golfers Entering Treated Turf Areas

Re-entry activity	Peak TTR (µg/cm^2)[1]	Transfer coefficient (cm^2/hr)[2]	Dermal exposure (mg/kg bw/day)[3]	Calculated MOE[4]	REI
Golfing – adults (16+)	0.0307	5300	8.13E-03	36,900	Until spray has dried
Golfing – youth (11-<16)	0.0307	4400	9.50E-03	31,600	
Golfing – child (6-<11)	0.0307	2900	1.11E-02	27,000	

[1] Calculated using the default for turf of 1% dislodgeable on the day of application and 10% dissipation per day
[2] Transfer coefficients obtained from 2012 US EPA Residential SOP for golfer exposure.
[3] Exposure = (Peak TTR [µg/cm^2] × TC [cm^2/hr] × Exposure Duration (4 hours for golfers) / ([80 kg bw for adults, 57 kg bw for youths and 32 kg bw for children] × 1000 µg/mg)
[4] Based on NOAEL of 300 mg/kg bw/day, target MOE = 100

3.4.3.3 Aggregate Exposure

Fluopyram is used on food crops and on golf courses. However, given that there were no common adverse effects between the toxicological endpoints for short- to intermediate-term dermal exposure and chronic dietary exposure to fluopyram (please refer to PRD2016-05, *Fluopyram* and ERC2014-02, *Fluopyram* for more details), an aggregate risk assessment was not conducted for these scenarios.

3.4.3.4 Bystander Exposure and Risk

Bystanders are not expected to be inside greenhouses while treatments occur; therefore, exposures are not expected for bystanders from the use of Fluopyram Greenhouse Fungicide. In addition for Fluopyram ST, bystander exposure should be negligible since the potential for drift is expected to be minimal when planting Fluopyram ST-treated seed.

Bystander exposure to FLU+TFS 1:1 SC Fungicide should be negligible since the potential for drift is expected to be minimal from the use of this product. Application is limited to sod farms and golf courses only when there is low risk of drift to areas of human habitation or activity (excluding golf courses) such as houses, cottages, schools and recreational areas including parks, school grounds, and playing fields is minimal, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

Fluopyram is registered for foliar/soil treatment on various field crops. Please refer to ERC2014-02, *Fluopyram* and PRD2016-05, *Fluopyram* for the residue definition for risk assessment and enforcement purposes, the residue trial data on soybeans treated foliarly, the residue trial data on field tomatoes, field peppers, field cucumbers and field lettuce, and the frozen storage stability of fluopyram in plant and animal foodstuffs. The information captured herein relates only to the seed treatment use on soybeans, and the greenhouse use on tomatoes, peppers, cucumbers and lettuce.

As determined in ERC2014-02, *Fluopyram*, the residue definition for enforcement is fluopyram in plant commodities, and the residue definition for risk assessment is fluopyram including the metabolite fluopyram-benzamide in crops of Crop Group 6 (Legume Vegetables) and 20 (Oilseeds), and fluopyram in all other plant commodities. Based on additional seed treatment wheat metabolism data, these residue definitions are also applicable to represent the residues resulting in/on crop commodities from seed treatment with fluopyram.

Crop field trials conducted throughout the United States, including Canadian representative growing regions, using end-use products containing fluopyram at approved rates in or on soybeans as a seed treatment are sufficient to support the proposed MRL on soybeans. Residue trials conducted in greenhouses in Europe using end-use products containing fluopyram at approved or exaggerated rates in or on tomatoes and cucumbers are sufficient to support the proposed MRLs on these crops. Based on crop grouping principles and residue data generated following foliar applications in fields, MRLs to cover residues of fluopyram are under promulgation at 4 ppm for peppers, and 40 ppm for lettuce. The use of fluopyram in greenhouses on these crops is not expected to result in residues exceeding these MRLs.

3.5.2 Exposure from Drinking Water

The following sections review the estimated environmental concentrations (EECs) of fluopyram resulting from water modelling. No monitoring data was available for fluopyram.

3.5.2.1 Concentrations in Drinking Water

Application Information and Model Inputs

Fluopyram is a fungicide with a maximum annual application rate of 500 g a.i./ha, applied as two applications of 250 g ai/ha, at 7-day intervals. Application information and the main environmental fate characteristics used in the models are summarized in Table 3.5.2-1.

Estimated environmental concentrations (EECs) of fluopyram in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of fluopyram in groundwater were calculated using the PRZM-GW model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PRZM-GW are average concentrations in the top 1m of the water table. EECs of fluopyram in surface water were calculated using the SWCC model, which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in a vulnerable drinking water source, a small reservoir.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EEC estimates are expected to allow for future use expansion into other crops at this application rate. Thirteen initial application dates for surface water and three dates for groundwater between April and July were modelled. The model was run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Table 3.5.2-2 below.

Table 3.5.2-1: Major groundwater and surface water model inputs for Level 1 assessment of fluopyram

Type of Input	Parameter	Value
Application	Maximum allowable application rate per year (g a.i./ha)	500
	Maximum rate each application (g a.i./ha)	250
	Maximum number of applications per year	2
	Minimum interval between applications (days)	7
	Method of application	Aerial
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	Stable
	Photolysis half-life in water (days)	Stable
	Adsorption K_{oc} (mL/g)	284 (20th percentile of 5 K_{oc} values)
	Aerobic soil biotransformation half-life at 20°C (days)	533 (80th percentile of a lognormal distribution fitted to seven half-lives)
	Aerobic aquatic biotransformation half-life at 20°C (days)	1330 (longer of two systems, average of two labels)
	Anaerobic aquatic biotransformation half-life at 20°C (days)	1495 (average of two labels)

Table 3.5.2-2: Level 1 estimated environmental concentrations of fluopyram in potential drinking water sources

Compound	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)	
			Reservoir	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
Fluopyram	72	72	25	5.1

1 90th percentile of daily average concentrations
2 90th percentile of 365-day moving average concentrations
3 90th percentile of the peak concentrations from each year
4 90th percentile of yearly average concentrations

3.5.3 Dietary Risk Assessment

Acute and chronic (cancer and non-cancer) dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™).

3.5.3.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the refined chronic cancer and non-cancer analysis for fluopyram: Supervised trial median residue (STMdR) values, experimental processing factors where available, updated Canadian projected percent crop treated values, and anticipated residues for livestock commodities. The refined chronic dietary exposure from all supported fluopyram food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 81% of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to fluopyram from food and water is 33.1% (0.003973 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1-2 years old at 97.4% (0.011683 mg/kg bw/day) of the ADI.

3.5.3.2 Acute Dietary Exposure Results and Characterization

The following criteria were applied in the refined acute analysis for fluopyram: Highest average field trial (HAFT) values, the assumption that 100% of crop is treated, experimental processing factors where available, and anticipated residues for livestock commodities. The refined acute dietary exposure from all supported fluopyram food uses was estimated to be 12.3% of the ARfD for the general population (95th percentile, deterministic). Aggregate exposure from food and water is considered acceptable and below PMRA's level of concern. Specifically, an acute dietary exposure of 7.8% to 37.0% of the ARfD was obtained for all population subgroups, with children 1-2 years old as the highest exposed population subgroup.

3.5.4 Aggregate Exposure and Risk

Although there is a residential use on turf, the dermal and oral exposures were not combined, as the dermal and oral acute toxicological endpoints are based on different toxicological effects.

3.5.5 Maximum Residue Limits

Table 3.5.5.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Crop Subgroup 8-09A (Tomatoes)	1
Crop Subgroup 9B (Squash/Cucumber)	0.6
Dry soybeans	0.3

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 Health Canada's website.

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

Please refer to ERC2014-02, *Fluopyram* and PRD2016-05, *Fluopyram* for the nature of the residues in animal and plant matrices, analytical methodology and field trial data for fluopyram. The nature of the residues in wheat from seed treatment, residue data from seed treatment trials in soybeans and greenhouse trials on tomatoes, peppers, cucumbers and lettuce, and acute and chronic (cancer and non-cancer) dietary risk estimates are summarized in Tables 1 and 2 in Appendix I.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Refer to ERC2014-02, *Fluopyram* and PRD2016-05, *Fluopyram* for details on physico-chemical properties, fate and behaviour of fluopyram in terrestrial and aquatic systems.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. The estimated environmental concentrations (EECs) are concentration of a pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e., protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify products and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints.

A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1 for most species, 0.4 for pollinators and 2 for beneficial arthropods). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk

assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risk Characterization for FLU+TFS 1:1 SC Fungicide

As the minimum application interval for this turf product is larger than what was previously assessed, the total cumulative rate in the environment is expected to be equal to, or lower than the previously registered use pattern, and the risk was not re-assessed. Refer to PMRA ERC2014-02, *Fluopyram* for details on the toxicity effects and risk assessment for fluopyram. Also refer to PMRA REG2004-03 for details on the toxicity effects and risk assessment for trifloxystrobin.

The proposed application rate of trifloxystrobin (500 g TFS/ha (two applications)) is lower than the currently registered use. In Compass 50WG Fungicide there is a maximum of two sequential applications of 305 g a.i./ha each and a total seasonal rate of 1200 g a.i./year. Therefore, buffer zones were recalculated for this petition. This new assessment indicates that buffer zones ranging from 1 to 5 m are required to protect the terrestrial and aquatic organisms from the uses.

The assessment of the environmental risk of trifloxystrobin with the uses of FLU+TFS 1:1 SC Fungicide identified concerns for wild birds, aquatic organisms and non-target terrestrial plants. Therefore, environmental hazard statements as found in the currently registered label of Compass 50WG Fungicide are also required on the FLU+TFS 1:1 SC Fungicide label.

4.2.2 Risk Characterization for Fluopyram Greenhouse Fungicide

Fluopyram Greenhouse Fungicide is used for the control of grey mould, botrytis leaf blight, botrytis stem canker, botrytis rot and powdery mildew diseases in greenhouse cucumbers, peppers, tomatoes and lettuce with a maximum application rate of 500 mL EP/ha (250 g a.i./ha) and repeated twice with an interval of 7-14 days. It is applied by foliar broadcast and drip/drench applications in the case of tomatoes. In the case of powdery mildew (100 mL EP/ha) and early blight (300 mL EP/ha), the applications are repeated three times. In all the cases, maximum seasonal rate is 1 L EP/ha (500 g a.i./ha).

This product is similar to a fluopyram product previously registered and evaluated in ERC2014-02, *Fluopyram*. The maximum application rate for the current greenhouse uses is the same as for the precedent product. Exposure to terrestrial organisms such as wild birds and mammals, soil organisms, predators and parasites, beneficial insects and non-target terrestrial plants is limited with the greenhouse uses, thus the risk to these organisms was not assessed.

Potential exposure to aquatic organisms by greenhouse use may come from discharge of effluents or limited run-off water from the greenhouses. A risk assessment conducted with fluopyram to aquatic organisms under a previous application (for details refer to ERC2014-02, *Fluopyram*) indicated that the level of concern was not exceeded for freshwater and marine fish, invertebrates and plants. A potential risk was, however, identified for amphibians at the screening level. A refined risk assessment with runoff water from treated fields indicated that the level of concern was slightly exceeded for amphibians (acute and chronic RQ were 1.68 and

1.93, respectively). Considering low RQ values and minimal runoff water from greenhouses, this scenario is unlikely to occur. The use of Fluopyram Greenhouse Fungicide, therefore, poses a negligible risk to amphibians.

Precautionary label statements are, however, required in order to not contaminate aquatic systems through discharge of effluents from the treated greenhouses.

4.2.3 Risk Characterization for Fluopyram ST

Fluopyram ST is a broad spectrum systemic fungicide with fluopyram as the technical active (600 g/L). Fluopyram ST is to be applied to soybean seeds using commercial slurry or mist-type seed treatment equipment at a rate of 0.15–0.25 mg a.i./seed. With a maximum seeding rate of 7400 seeds per kg and 126 kg of seed/ha, the maximum seasonal application rate is equal to 233 g a.i. fluopyram/ha. Please see Appendix I, Tables 5 to 9 for details on the risk assessment.

4.2.4 Risks to Terrestrial Organisms

A risk assessment to non-target terrestrial organisms was conducted with fluopyram under a previous application at a rate of 500 g a.i/ha (for details refer to ERC2014-02, *Fluopyram*). This assessment indicated that fluopyram will pose a negligible risk to soil organisms, predators and parasites and bees at an application rate of 500 g a.i./ha. As the application rates in the end-use products are lower than those previously reviewed and published under ERC2014-02, *Fluopyram*, risk to these organisms was not re-assessed.

Wild birds and mammals

The risk to these organisms was re-assessed since seed treatment is a new use for fluopyram.

To characterize the risk to birds and mammals, the likelihood of exceeding the toxic effects endpoints through feeding on treated seed was considered. The initial risk was thus characterized using the risk quotient method (RQ = estimated exposure/toxicity endpoint). The risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, a refined risk assessment is performed to further characterize the risk.

In order to characterize the risk, both the estimated exposures and toxicity endpoints must be expressed in the same units. In this risk assessment, exposure and toxicity were expressed as a number of seeds consumed per day.

The exposure of birds and mammals to a pesticide through consumption of treated seed is a function of the amount of pesticide on the seed, the body weight and food ingestion rate of the bird/animal, and the number of seeds available for consumption. As an initial conservative screening scenario, risk was characterized for generic small, medium, and large size classes of birds and wild mammals. For the screening level assessment, it was assumed that treated seed would be available for consumption over an extended time period and that 100% of the diet

would consist of treated seed. Variables of feeding preference, availability of treated seed, or potential avoidance behaviour toward treated seed were not considered at the screening level.

Exposure was estimated using the following equation:

> Estimated daily exposure (expressed as number of seeds consumed per day) = Number of seeds/g of seeds x Food Ingestion Rate (g dw diet/day)

The rates of fluopyram expressed as active ingredient per kg of seed, number of seeds per kg, and seeding rate in kg/ha are provided in Appendix I. Based on seeding rate and active ingredient per kg, application rate per hectare was calculated to be 78 to 233 g a.i./ha.

The Food Ingestion Rate (FIR) is based on allometric equations from Nagy (1987). These equations determine the mass of food consumed per day in dry weight, based on the body weight of the organism. The estimated daily exposure in mg a.i./kg bw/day, calculated with number of seeds per gram and FIR, can be found in Appendix I, Tables 5 to 9.

The number of seeds that must be consumed per day to reach the toxicity endpoint was determined using the following equation:

Number of seeds consumed per day to reach the toxicity endpoint = Daily dose (mg a.i./kg bw or mg a.i./kg bw/day) x generic body weight of organism (kg) ÷ Amount of active ingredient per seed (mg a.i./seed).

Assessment of risk to birds on an acute basis: The acute LD_{50} for bobwhite quail was 2000 mg a.i./kg bw. The RQ values, calculated by applying an uncertainty factor of 10, were 2.3, 1.8 and 0.5 for the small, medium and large birds, respectively. These values indicate that the RQs for small and medium birds slightly exceeded level of concern and therefore, these birds are expected to be at low risk on an acute basis with the uses.

Assessment of risk to bird's reproduction: The most sensitive species to reproductive performance is bobwhite quail with a NOAEC of 46.7 mg a.i./kg diet, which amounts to a NOAEL of 4.12 mg a.i./kg bw/d. The RQ values with exposure to treated field exceeded the level of concern of 1, i.e., 114.0, 89.6 and 26.1 for small, medium and large sized birds, respectively. These values indicate that the uses of Fluopyram ST may pose a risk to reproductive performance of small, medium and large birds if exposed to treated seed in the treated field. Risk mitigations measures such as precautionary label statements are required to protect the wild birds.

Assessment of risk to mammals on an acute basis: The most sensitive species to acute exposure was the rat with an acute LD_{50} of 2000 mg a.i./kg bw. The RQ values, calculated by applying an uncertainty factor of 10, were 1.3, 1.2 and 0.6 for the small, medium and large mammals, respectively. These values indicate that the RQs for small and medium mammals slightly exceeded level of concern and therefore, mammals are expected to be at low risk on an acute basis with the uses.

Assessment of risk to mammal's reproduction: The most sensitive species to reproductive performance was the rat with an NOAEL of 13.9 mg a.i./kg bw/d. The RQ values with exposure to treated field exceeded the level of concern, i.e., 19.3, 16.6 and 9.1 for small, medium and large sized mammals, respectively. These values indicate that the uses of Fluopyram ST may pose a risk to reproductive performance of small, medium and large wild mammals if exposed to treated seed in the field. Risk mitigations measures such as precautionary label statements are required to protect small mammals.

Refined risk assessment: The above screening level risk assessment assumes no dissipation of the active ingredient from the treated seed, and that the seeds will be available for consumption by foraging birds and mammals. Under field conditions, however, some dissipation of the active ingredient from the surface of the treated seeds is expected to occur at planting and from contact with soil and water. Actual exposure may be further reduced since the availability of seeds to foraging birds and mammals is affected by various factors including the number of seeds per unit area and whether planted seeds are buried or exposed.

Further characterization of risk for birds: During the study of the possible role of ultraviolet reflection in seed colour preferences and repellent strategies, Smith (2006) reported that soybean seed was not attractive to birds and that none of the species were observed consuming soybean. Based on this evidence, it was determined that when used in according to label directions, the use of fluopyram as a fungicide on soybean seed will pose a negligible risk to birds.

Further characterization of risk for small mammals: The end-point used to conduct the mammalian reproduction risk assessment was based on a multi-generation, daily dietary exposure NOEL of 50 mg a.i./kg diet (13.9 mg a.i./kg bw/day). The observed parameters of this NOEL were slight reductions (less than 10%) in body weight as well as other sub-lethal organ and hormonal effects. As soybeans have an approximate germination time of two weeks, treated seed would only be available for consumption for 14 days post planting. It is not anticipated that small mammals would consume treated seed for a consecutive 14 days. Furthermore, it is not anticipated that the small reduction in body weight and or other organ and hormone-level effects will have any impacts on the population levels of small mammals. Therefore, when used according to label directions, the use of fluopyram as a fungicide on soybean seed will pose a negligible risk to small mammals.

Label statements requiring the incorporation of seeds into soil and cleanup of spilled seeds will be required on the product label in order to help reduce exposure of non-target birds and mammals to the active ingredient.

Risk to terrestrial plants

A risk assessment for terrestrial plants conducted with fluopyram under a previous application indicated that the risk quotients exceeded the level of concern for seedling emergence and vegetative vigour with an application rate of 250 g a.i./ha and two applications with 7-day interval. The risk to terrestrial plants was, therefore, re-assessed with seed treatment application rate of 138.89 g a.i./ha.

Studies on toxicity/effects on seedling emergence and vegetative vigour indicated EC_{25} values of greater than 500 and 250 g a.i./ha (the highest applications rates tested), respectively. The RQ values were calculated using seed treatment application rate of 138.89 g a.i./ha. The low RQ values of 0.28 and 0.56 for seedling emergence and vegetative vigour, respectively, were less than the level of concern and, therefore, the use will pose a negligible risk to non-target terrestrial plants.

4.2.5 Risk to aquatic organisms

Risk to aquatic organisms with fluopyram was conducted with fluopyram under a previous application at an application rate of 500 g a.i./ha in. This assessment indicated that fluopyram will pose a negligible risk to freshwater and marine aquatic organisms including invertebrates, fish, algae and non-target plants at an application rate of 500 g a.i./ha by ground application. As the application rates in this product are lower than those previously assessed, risk to these organisms was not re-assesed.

Screening and refined risk asessments, however, indicated that the use of fluopyram at 500 g a.i./ha will pose a risk to amphibians and, therefore, risk to these organisms with the new uses in was re-assessed. Acute risk to amphibians was assessed using the acute LC_{50} of most sensitive fish species (rainbow trout, 1.78 mg a.i./L) with an uncertainty factor of 10. The chronic risk was assessed with fish chronic NOEC (fathead minnow, 0.135 mg a.i./L). The screening level EEC, estimated with an application rate of 138.89 g a.i./ha and a water depth of 15 cm, was 0.093 mg a.i./L. The RQ values for the acute and chronic exposure were less than one, i.e., 0.52 and 0.69, respectively. These low RQ values did not exceed the level of concern for the acute and chronic exposures and therefore, the use of Fluopyram ST for the soybean seed treatment will pose a negligeable risk to amphibians.

Risk mitigation

An assessment of the environmental risk with the use of Fluopyram ST has identified concerns to wild birds and mammals. Risk mitigation measures in the form of label statements are therefore required to protect the wild birds and mammals.

5.0 Value

5.1 Consideration of Benefits

The registration of fluopyram provides a new active ingredient for the management of certain economically important diseases that appear on the different end use product labels. This is of particular importance given reports of field resistance to currently registered alternative active ingredients in some of the labelled diseases.

In the case of FLU + TFS 1:1 SC Fungicide, fluopyram provided industry accepted levels of control of dollar spot on highly managed turf under moderate to high disease pressure. Currently, several alternative fungicide products are registered in Canada to control summer diseases including fungicides from groups 1, 2, 3, 7, 11, and M. However, the dollar spot pathogen has

developed resistance to actives in groups 1, 2, and 3. The addition of a new group 7 active ingredient, fluopyram, in fungicide programs will offer an alternative chemistry to control dollar spot on golf courses and lower the risk of resistance development towards that disease. In addition, trifloxystrobin, registered in the fungicide Compass 50 WG for control of brown patch and leaf spot on turfgrass, will broaden the disease spectrum of FLU + TFS 1:1 SC Fungicide.

Fluopyram ST, the seed treatment product, provides control of sudden death syndrome (SDS) caused by *Fusarium virguliforme* in soybean. Soybean is an economically important crop in Canada and SDS has become a prominent and economically important disease in southwestern Ontario. In some areas, SDS now ranks among the top-tier of yield-reducing diseases of soybean. Currently, only one other product, Heads Up Plant Protectant (quinoa extracts), is registered to suppress SDS of soybean in Canada.

Fluopyram Greenhouse Fungicide controls major fungal diseases that have the potential to severely reduce yield in Canadian greenhouse vegetable production. The claims appearing on the product label cover the four greenhouse vegetable crops with the largest production areas in Canada; tomato, pepper, cucumber, and lettuce. Registration of Fluopyram Greenhouse Fungicide provides greenhouse growers with an additional end-use product option against diseases in high value crops where relatively few alternatives are currently available (see Appendix I, Table 20). In addition, Fluopyram Greenhouse Fungicide is the first product with label recommendations for drip/drench applications to manage grey mould in greenhouse tomatoes. Access to this method of application is of particular value given the high reliance on hydroponic production systems in greenhouse tomato production.

5.2 Effectiveness Against Pests

FLU + TFS 1:1 SC Fungicide for use on turf

Value information was submitted in the form of efficacy trials and scientific rationales. It was demonstrated in the efficacy trials that the control of the dollar spot is done by the fluopyram component. The active trifloxystrobin is the component effective in controlling the other diseases (i.e. brown patch and leaf spot). Trifloxystrobin is registered to control brown patch and leaf spot at the same rates and application intervals as in the fungicide product Compass 50WG Fungicide. Therefore, the application of FLU + TFS 1:1 SC Fungicide in a preventative fungicide program will broaden the disease spectrum by treating for dollar spot, and the trifloxystrobin component of the product will manage brown patch and leaf spot if present at the same time.

Fluopyram ST for use on soybean

Value information was submitted in the form of efficacy trials and scientific rationales. Fluopyram applied at 0.15–0.25 mg active ingredient/seed provided acceptable control of SDS and increased yield significantly.

Fluopyram Greenhouse Fungicide for use on greenhouse vegetables (cucumber, pepper, tomato, and lettuce)

The efficacy of Fluopyram Greenhouse Fungicide in controlling major greenhouse vegetable diseases was demonstrated in a series of small scale greenhouse trials on the labelled crops or through scientific rationales that allowed extrapolation of evidence from trials conducted on other crops. Diseases shown to be controlled by Fluopyram Greenhouse Fungicide included botrytis/grey mould, powdery mildew and early blight. Although trials were located outside of North America, their results were deemed relevant to the Canadian context given the controlled greenhouse conditions under which they were conducted. The efficacy of the product when applied as a drench or drip treatment on tomato was equally demonstrated in a series of ten greenhouse trials. These trials demonstrated that this method of application was equivalently effective in controlling botrytis in tomato when compared to foliar applications.

5.3 Non-Safety Adverse Effects

Phytotoxicity was not observed in any of the trials conducted on turf, soybean or greenhouse crops when any of the fluopyram-containing products were applied.

5.4 Supported Uses

The reviewed value information is sufficient to support the claims on the different fluopyram-containing-fungicide products. Details of the supported uses are provided in Appendix I, Table 21.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

For full details, please refer to PRD2016-05, *Fluopyram* and ERC2014-02, *Fluopyram*.

6.2 Formulants and Contaminants of Health or Environmental Concern

For full details, please refer to PRD2016-05, *Fluopyram* and ERC2014-02, *Fluopyram*.

7.0 Summary

7.1 Human Health and Safety

Mixers, loaders and applicators handling products containing fluopyram, workers re-entering treated areas or handling treated seed, and golfers re-entering treated golf courses are not expected to be exposed to levels of fluopyram that will result in health risks of concern when the products are used according to label directions. The personal protective equipment on the product label is adequate to protect workers. For full details, please refer to PRD2016-05, *Fluopyram* and ERC2014-02, *Fluopyram*.

The nature of the residues in plants is adequately understood, including metabolic pathways resulting from seed treatment. The residue definition for enforcement is fluopyram in plant commodities, and the residue definition for risk assessment is fluopyram including the metabolite fluopyram-benzamide in crops of Crop Group 6 (Legume Vegetables) and 20 (Oilseeds), and fluopyram in all other plant commodities. The use of fluopyram as a seed treatment on soybeans, and in greenhouses on tomatoes, peppers, cucumbers and lettuce does not constitute a health risk of concern for chronic or acute dietary exposure (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend MRLs. The PMRA recommends that the following MRLs be specified for residues of fluopyram.

Commodity	Recommended MRL (ppm)
Crop Subgroup 8-09A (Tomatoes)	1
Crop Subgroup 9B (Squash/Cucumber)	0.6
Dry soybeans	0.3

Based on crop grouping principles and residue data generated following foliar applications in fields, MRLs to cover residues of fluopyram are under promulgation at 4 ppm for peppers, and 40 ppm for lettuce. The use of fluopyram in greenhouses on these crops is not expected to result in residues exceeding these MRLs.

7.2 Environmental Risk

When used according to label directions, fluopyram does not present risks of concerns to the environment. Fluopyram is persistent in soils and has a potential for long-term accumulation and residue carryover to the following crop season. Fluopyram is stable to hydrolysis, photolysis, aerobic and anaerobic biotransformation in soils. It does not form major transformation products in soils under Canadian field use conditions. Fluopyram is moderately mobile in soils and has a potential to leach and contaminate the groundwater depending on the soil type and location. Fluopyram has a low potential for bioconcentration/bioaccumulation in organisms.

Fluopyram is persistent in aquatic systems under aerobic and anaerobic conditions. Photolysis is not an important route of transformation in the aquatic environment. It does not form major transformation products in the water or sediment phases. Several minor transformation products were detected in natural water of which one was identified as fluopyram-lactam.

Fluopyram has a low potential for volatilization and, therefore, is not expected to result in long range transport in the atmosphere.

Fluopyram presents a negligible risk to soil organisms, bees, beneficial arthropods, freshwater and marine fish, invertebrates, algae and aquatic plants. Fluopyram, however, may pose a risk to non-target terrestrial plants from spray drift and to amphibians due to runoff and spray drift from the use of FLU+TFS 1:1 SC Fungicide. Fluopyram may also pose a risk to non-target wild birds and small mammals from the ingestion of seed treated with Fluopyram ST.

In order to minimize the potential risk, spray buffer zones between the treated area and downwind sensitive terrestrial and aquatic habitats are required for FLU+TFS 1:1 SC Fungicide as well as precaution statements for non-target terrestrial plants, non-target aquatic organisms, wild birds and small mammals. Risk mitigation and precaution label statements for wild birds and small mammals are required to reduce possible risks from seed treated with Fluopyram ST. Precaution statements for non-target aquatic organisms and greenhouse effluent statements are required for Fluopyram Greenhouse Fungicide.

7.3 Value

The value information provided to support the registration of the fluopyram-containing products was primarily in the form of efficacy trials along with scientific rationales. The level of efficacy against the pathogens in the trials was deemed acceptable and comparable to the commercial standards tested. The majority of the diseases in question are of major economic and agricultural importance in Canada. Inclusion of fluopyram in fungicide programs will provide Canadian growers with additional end-use product options and, for some of the labeled diseases, an alternative active ingredient with a mode of action that is different from those that are currently registered. In such cases, fluopyram will be beneficial to disease resistance management.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Fluopyram Technical Fungicide and three end-use products, FLU+TFS 1 :1 SC fungicide containing the technical grade active ingredients fluopyram and trifloxystrobin, Fluopyram ST, and Fluopyram Greenhouse Fungicide, containing the technical grade active ingredient fluopyram. All three end-use products are used to control several fungal diseases on turf, soybean seeds or food crops.

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

List of Abbreviations

♀	female
♂	male
λ	wavelength
µg	microgram
µm	micrometre
a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
ATPD	area treated per day
BCF	bioconcentration factor
bw	body weight
CAF	composite assessment factor
cm	centimetre
C_{max}	maximum concentration
d	day(s)
DACO	data code
DAP	days after planting
DFR	dislodgeable foliar residue
EC	emulsion
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
ECH	earliest commercial harvest
EDE	estimated daily exposure
EEC	estimated environmental concentration
EP	end-use product
FDA	*Food and Drugs Act*
FRAC	fungicide resistance action committee
g	gram
GC-MS	gas chromatography mass spectroscopy
GLP	Good Laboratory Practice
ha	hectare
HAFT	highest average field trial
hr	hour
IOM	Institute of Occupational Medicine
J	Joul
K	Henry's Law Constant
kg	kilogram
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	n–octanol-water partition coefficient
L	litre
LAFT	lowest average field trial
lb	pound
LC_{50}	lethal concentration 50%

LD_{50}	lethal dose 50%
LLNA	local lymph node assay
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
m^2	square metre
MAS	maximum average score
mg	milligram
MIS	maximum irritation score
mL	millilitre
mm	millimetre
mmHg	millimetre of mercury
MOA	mode of action
MOE	margin of exposure
mol	mole
MRL	maximum residue limit
mw	molecular weight
n	number of field trials
N/A	not applicable
nm	nanometre
NOAEC	no observed adverse effect concentration
NOAEL	no observable adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OECD	Organization for Economic Cooperation and Development
ORETF	Outdoor Residential Exposure Task Force
OSHA	Occupational Safety & Health Administration
Pa	Pascal
PCPA	*Pest Control Product Act*
pH	measure of the acidity or basicity of an aqueous solution
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
q_1*	cancer potency factor
RA	risk assessment
REI	restricted entry interval
RQ	risk quotient
SD	standard deviation
SDS	sudden death syndrome
STMdRs	supervised trial median residue
STMR	supervised trial mean residue
TC	transfer coefficient
TGAI	technical grade active ingredient

TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
TTR	transferable turf residue
USEPA	United States Environmental Protection Agency
USFDA	United States Food and Drug Administration
UV	ultraviolet
v/v	volume per volume dilution
w/v	weight per volume dilution
w/w	weight per weight dilution
wt	weight
yr	year

Appendix I Tables and Figures

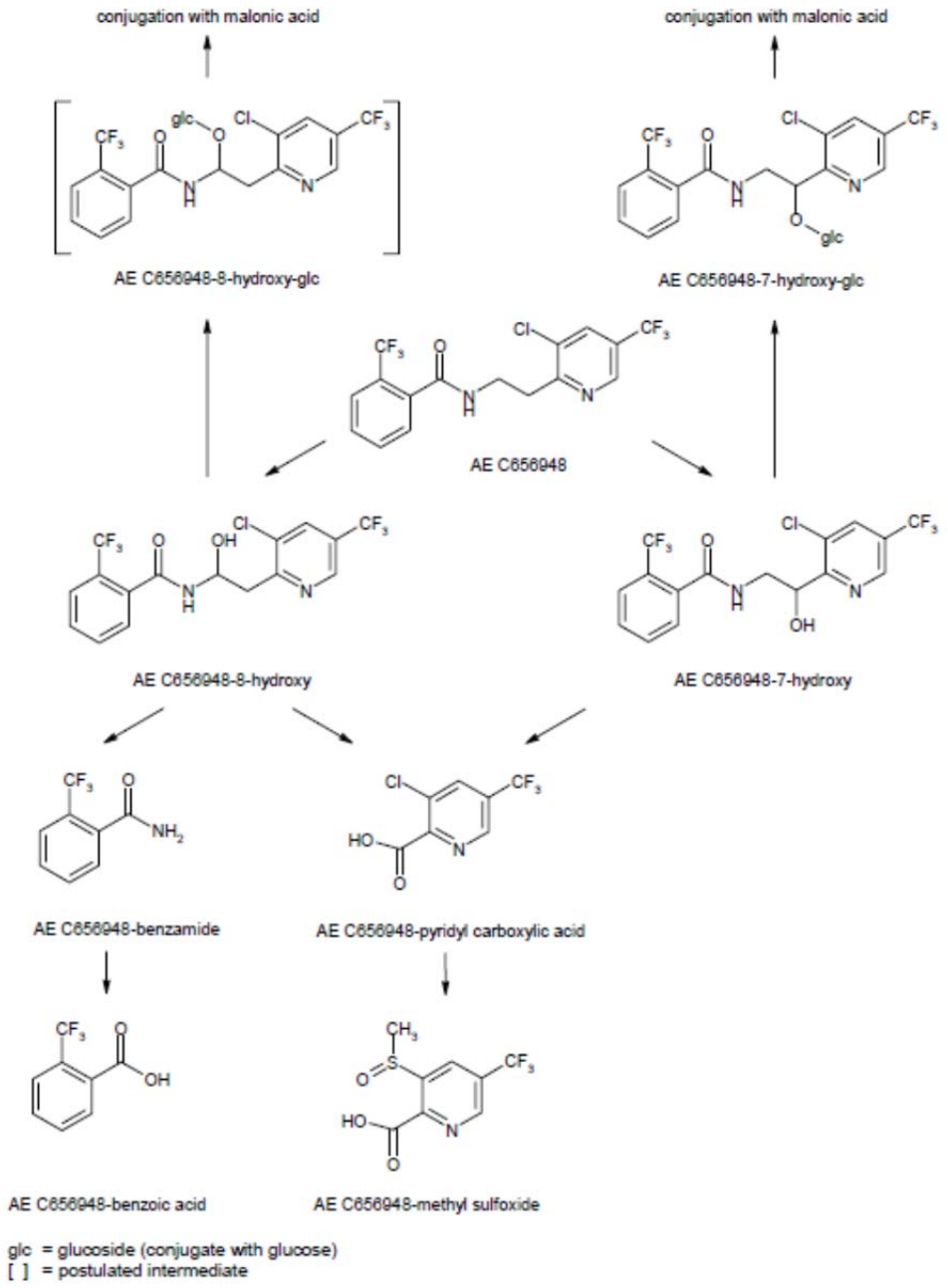
Table 1 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN WHEAT – SEED TREATMENT			PMRA# 2329907	
Radiolabel Position	[Phenyl-U-^{14}C] and [Pyridyl-2,6-^{14}C]			
Test Site	In containers in a covered vegetation area; one container per label (1 m^2 surface area per container)			
Treatment	Seed treatment			
Total Rate	Phenyl-label: 10.5 g ai/100 kg seed (18.1 g ai/ha) Pyridyl-label: 10.8 g ai/100 kg seed (18.6 g ai/ha)			
Formulation	Flowable concentrate for seed treatment (FS) formulation			
Days after planting (DAP)	Wheat forage: 40 DAP (BBCH 30); Wheat hay: 79 DAP (BBCH 77-83); Wheat straw and grain: 112 DAP (at maturity; BBCH 89-92))			
Matrices	**DAP (days)**	**[Phenyl-U-^{14}C]**	**[Pyridyl-2,6-^{14}C]**	
		TRRs (ppm)	**TRRs (ppm)**	
Forage	40	0.132	0.142	
Hay	79	0.238	0.287	
Straw	112	0.506	0.477	
Grain	112	0.006	0.012	
Metabolites Identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[Phenyl-U-^{14}C]**	**[Pyridyl-2,6-^{14}C]**	**[Phenyl-U-^{14}C]**	**[Pyridyl-2,6-^{14}C]**
Forage	Fluopyram; AE C656948-7-hydroxy-glc-MA	Fluopyram; AE C656948-7-hydroxy-glc-MA	AE C656948-benzamide; AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc (-8-hydroxy-glc-SA); AE C656948-8-hydroxy; AE C656948-8-hydroxy-glc-MA	AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc; AE C656948-8-hydroxy; AE C656948-8-hydroxy-glc-MA; AE C656948-pyridyl-carboxylic acid
Hay	Fluopyram; AE C656948-benzamide; AE C656948-7-hydroxy-glc-MA	Fluopyram; AE C656948-7-hydroxy-glc-MA	AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc (-8-hydroxy-glc-SA); AE C656948-8-hydroxy-glc-MA	AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc; AE C656948-8-hydroxy; AE C656948-8-hydroxy-glc-MA; AE C656948-pyridyl-carboxylic acid
Straw	Fluopyram; AE C656948-7-hydroxy-glc-MA	Fluopyram; AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc-MA	AE C656948-benzamide; AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc (-8-hydroxy-glc-SA); AE C656948-8-hydroxy; AE C656948-8-hydroxy-glc-MA	AE C656948-7-hydroxy-glc; AE C656948-8-hydroxy; AE C656948-8-hydroxy-glc-MA; AE C656948-methyl sulfoxide
Grain	Fluopyram; AE C656948-benzamide; Unknowns	Fluopyram; Unknowns	AE C656948-7-hydroxy; AE C656948-benzoic acid	None

Proposed Metabolic Scheme in Plants

Metabolism of fluopyram in wheat proceeds mainly via hydroxylation of the ethyl-linking group to form AE C656948-7-hydroxy (major extent) or AE C656948-8-hydroxy (minor extent). These metabolites subsequently undergo either: (1) conjugation with glucose and subsequently malonic acid or others to yield AE C656948-7-hydroxy-glc, AE C656948-7-hydroxy-glc-MA, AE C656948-8-hydroxy-glc-MA, and possibly AE C656948-8-hydroxy-glc-SA; or (2) cleavage to

yield AE C656948-benzamide, AE C656948-benzoic acid, and AE C656948-pyridyl-acetic acid, and via substitution of the pyridyl chlorine, AE C656948-methyl-sulfoxide.



CROP FIELD TRIALS & RESIDUE DECLINE ON SOYBEANS {SEED TREATMENT}	PMRA# 2329922

Twenty-one residue trials were conducted on soybeans in 2012 in the United States, including Canadian representative growing regions. Trials were conducted in NAFTA Growing Regions 2 (2 trials), 4 (3 trials) and 5 (16 trials). Each trial consisted of one untreated plot and three treated plots, reflecting application of fluopyram made either as a seed treatment (TRTST1 and TRTST2) or as a seed treatment followed by two foliar applications (TRTG1). A bridging study was conducted in three trials, reflecting two foliar applications (TRTG2). A suspension concentrate (SC) formulation of fluopyram was used for seed treatment and foliar applications. Seed was treated using commercial seed treatment procedures. Foliar broadcast applications were made using ground equipment in spray volumes of 92-187 L/ha. A nonionic surfactant, crop oil concentrate, or methylated seed oil was added to the spray mixture for foliar applications. Treated seed was planted at all plots within 88 days of treatment. At the TRTG1 plots, the re-treatment intervals (RTIs) were 90-131 days between planting and first foliar application, and 5-8 days between the first and second foliar applications. For TRTG2, two foliar applications were made with a 6- to 8-day RTI. Samples of soybean seed were harvested at maturity/earliest commercial harvest (ECH).

At two trials, samples were collected to assess residue decline at PHIs of 120/145, 127/148, 132/155, and 138/159 days (TRTST1 and TRTST2), and at PHIs of 3, 10, 15/17, and 21 days (TRTG1). In the TRTST1 and TRTST2 decline plots, residues of fluopyram remained constant with increasing PHI in soybean seed. In the TRTG1 decline plots, residues of fluopyram increased from 0.0194 and 0.0794 ppm at a 3-day PHI to 0.0341 and 0.1797 ppm at a 10-day PHI, and then generally declined with increasing PHIs. Residues of fluopyram-benzamide were ≤LOQ in/on all samples of soybean seed from the TRTST1 and TRTST2 decline plots and one TRTG1 decline plot; therefore decline could not be assessed. In one TRTG1 decline plot, residues increased with increasing PHI; residues of fluopyram-benzamide increased from <0.0102 ppm at a 3-day PHI to 0.0512 ppm at a 21-day PHI.

Commodity	Total Application Rate	PHI (days)	Residue Levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SD
Fluopyram								
Soybean seed, dry	TRTST1: 0.25 mg ai/seed (0.065-0.161 kg ai/ha)	110-152	21	<0.01	0.0271	0.01	0.0137	0.0059
	TRTST2: 0.15 mg ai/seed (0.038-0.097 kg ai/ha)	82-152	21	<0.01	0.0201	0.01	0.0111	0.0026
	TRTG1: 0.25 mg ai/seed (0.064-0.161 kg ai/ha) + 0.112-0.119 kg ai/ha (foliar) + 0.248-0.261 kg ai/ha (foliar) Total: 0.43-0.53 kg ai/ha	12-24	21	<0.01	0.2102	0.0219	0.0448	0.0545
	TRTG2: 0.245-0.256 kg ai/ha x 2 (foliar) Total: 0.49-0.51 kg ai/ha	13-14	3	<0.01	<0.0123	0.010	0.0108	0.0013
2-(trifluoromethyl)benzamide, reported in fluopyram equivalents								
Soybean seed, dry	TRTST1: 0.25 mg ai/seed (0.065-0.161 kg ai/ha)	110-152	21	<0.01	<0.01	0.01	0.01	NA
	TRTST2: 0.15 mg ai/seed (0.038-0.097 kg ai/ha)	82-152	21	<0.01	<0.01	0.01	0.01	NA
	TRTG1: 0.25 mg ai/seed (0.064-0.161 kg ai/ha) + 0.112-0.119 kg ai/ha (foliar) + 0.248-0.261 kg ai/ha (foliar) Total: 0.43-0.53 kg ai/ha	12-24	21	<0.01	0.0368	0.01	0.0113	0.0058
	TRTG2: 0.245-0.256 kg ai/ha x 2 (foliar) Total: 0.49-0.51 kg ai/ha	13-14	3	<0.01	<0.01	0.01	0.01	NA

LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation
Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ.
n = number of independent field trials

CROP FIELD TRIALS & RESIDUE DECLINE ON GREENHOUSE TOMATOES	PMRA# 1599669, 1599644, 2427649 and 2427642

Twelve residue trials were conducted on standard sized/cherry tomatoes in 2006 and 2007 in greenhouses in France, Spain, Italy, Germany, Netherlands, Greece and Portugal. The formulation AE C656948 SC 500 was applied twice at an application rate of 300 g ai/ha, for a total of 600 g ai/ha. The applications were made at intervals of 6-7 days, using ground equipment in spray volumes of 500-1500 L/ha. Residue decline data showed that residues of fluopyram decreased in greenhouse tomatoes with increasing PHIs from 0 to 7 days.

Seven residue trials were conducted on standard sized/cherry tomatoes in 2007 and 2008 in greenhouses in France, Spain, Netherlands, Italy and Germany. The formulation AE C656948 SC 500 was applied four times as a drip irrigation at an application rate of 500 g ai/ha, for a total of 2.0 kg ai/ha. The applications were made at intervals of 7-8 days, using water volumes of 1875 L/ha. Residue decline data showed that residues of fluopyram increased in greenhouse tomatoes with increasing PHIs from 0 to 7 days.

Commodity	Total Application Rate	PHI (days)	Residue Levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SD
Fluopyram								
Tomatoes (greenhouse)	0.6 kg ai/ha (foliar spray)	0	12	0.15	0.81	0.22	0.29	0.19
	2.0 kg ai/ha (drip)	0	7	0.01	0.23	0.11	0.11	0.08

LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation
Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ.
n = number of independent field trials

CROP FIELD TRIALS & RESIDUE DECLINE ON GREENHOUSE PEPPERS	PMRA# 1654357 and 1654355

Nine residue trials were conducted on bell/nonbell peppers in 2006 and 2007 in greenhouses in Germany, Netherlands, France, Italy, Spain, Greece and Portugal. The formulation AE C656948 SC 500 was applied twice at an application rate of 300 g ai/ha, for a total of 600 g ai/ha. The applications were made at intervals of 6-7 days, using ground equipment in spray volumes of 500-1500 L/ha. Residue decline data showed that residues of fluopyram decreased in greenhouse peppers with increasing PHIs from 0 to 7 days.

Commodity	Total Application Rate	PHI (days)	Residue Levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SD
Fluopyram								
Peppers (greenhouse)	0.6 kg ai/ha	0	9	0.24	0.72	0.42	0.43	0.14

LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation
Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ.
n = number of independent field trials

CROP FIELD TRIALS & RESIDUE DECLINE ON GREENHOUSE CUCUMBERS	PMRA# 1661218

Eight residue trials were conducted on cucumbers in 2006 in greenhouses in France, Spain, Italy, Germany, Netherlands and Greece. The formulation AE C656948 SC 500 was applied twice at an application rate of 300 g ai/ha, for a total of 600 g ai/ha. The applications were made at intervals of 6-7 days, using ground equipment in spray volumes of 500-1500 L/ha. Residue decline data showed that residues of fluopyram decreased in greenhouse cucumbers with increasing PHIs from 0 to 7 days.

Commodity	Total Application Rate	PHI (days)	Residue Levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SD
Fluopyram								
Cucumbers (greenhouse)	0.6 kg ai/ha	0	8	0.10	0.40	0.17	0.20	0.10

LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation
Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ.
n = number of independent field trials

CROP FIELD TRIALS & RESIDUE DECLINE ON GREENHOUSE LETTUCE	PMRA# 1661166 and 1661173

Twelve residue trials were conducted on head lettuce in 2006 and 2007 in greenhouses in France, Germany, Italy, Spain, Portugal and Greece. The formulation AE C656948 SC 500 was applied twice at an application rate of 250 g ai/ha for a total of 500 g ai/ha. The applications were made at intervals of 7 days, using ground equipment in spray volumes of 200-1000 L/ha. Residue decline data showed that residues of fluopyram decreased in greenhouse lettuce with increasing preharvest intervals (PHIs) from 7 to 14 days.

Commodity	Total Application Rate	PHI (days)	Residue Levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SD
Fluopyram								
Lettuce (greenhouse)	0.5 kg ai/ha	7	12	0.16	8.40	2.60	3.59	2.79

LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation
Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ.
n = number of independent field trials

Table 2 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (seed treatment - wheat)**		Fluopyram	
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops (seed treatment - wheat)**		Fluopyram including the metabolite fluopyram-benzamide in crops of Crop Group 6 (Legume Vegetables) and 20 (Oilseeds), and fluopyram in all other plant commodities	
METABOLIC PROFILE IN DIVERSE CROPS		Similar in grape, potato, beans, peppers (foliar application) and wheat (seed treatment)	
DIETARY RISK FROM FOOD AND WATER			
Refined chronic (cancer and non-cancer) dietary risk **ADI = 0.012 mg/kg bw/day** **Estimated chronic drinking water concentration = 72 µg a.i./L**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
	All infants < 1 year	24.7	70.0
	Children 1-2 years	80.7	97.4
	Children 3-5 years	51.7	65.2
	Children 6-12 years	29.6	39.7
	Youth 13-19 years	15.6	24.2
	Adults 20-49 years	16.2	28.2
	Adults 50+ years	16.9	28.6
	Females 13-49 years	16.0	27.8
	Total population	21.0	33.1
Refined acute dietary exposure analysis, 95th percentile **ARfD = 0.5 mg/kg bw** **Estimated acute drinking water concentration = 72 µg a.i./L**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
	All infants < 1 year	22.7	23.2
	Children 1-2 years	36.8	37.0
	Children 3-5 years	23.1	23.3
	Children 6-12 years	14.2	14.5
	Youth 13-19 years	8.2	8.4
	Adults 20-49 years	7.6	7.9

	Adults 50+ years	7.4	7.8
	Females 13-49 years	7.9	8.2
	Total population	12.3	12.8

Table 3 Toxicity Profile of FLU+TFS 1:1 SC Fungicide, Fluopyram ST and Fluopyram Greenhouse Fungicide

4Study Type/ Animal/ PMRA #	Study Results	Primary Display Panel Labelling
Acute Toxicity Studies – FLU+TFS 1:1 SC Fungicide		
Acute Oral LD_{50} Up and Down (425) PMRA 2427108	LD_{50} ♀ > 5000 mg/kg	No signal words required
Acute Dermal LD_{50} PMRA 2427112	LD_{50} ♂♀ > 5000 mg/kg	No signal words required
Acute Inhalation LC_{50} PMRA 2427114	LC_{50} ♂♀ > 4.62 mg/L	No signal words required
Primary Eye Irritation PMRA 2427116	MAS[a] = 2.4/110 MIS[b] = 5.3/110	No signal words required
Primary Skin Irritation PMRA 2427117	MAS[a] = 0.33/8 MIS[b] = 1/8	No signal words required
Skin Sensitization LLNA PMRA 2427119	EC3 = 36%	Potential – Skin Sensitizer
Acute Toxicity Studies – Fluopyram ST		
Acute Oral LD_{50} Up and Down (425) PMRA 2329898	LD_{50} ♀ = 1750 mg/kg	CAUTION – POISON
Acute Dermal LD_{50} PMRA 2329899	LD_{50} ♂♀ > 5000 mg/kg	No signal words required
Acute Inhalation LC_{50} PMRA 2329900	LC_{50} ♂♀ > 5.11 mg/L	No signal words required
Primary Eye Irritation PMRA 2329901	MAS[a] = 0/110 MIS[b] = 0/110	No signal words required

4Study Type/ Animal/ PMRA #	Study Results	Primary Display Panel Labelling
Primary Skin Irritation PMRA 2329902	MAS[a] = 0/8 MIS[b] = 0/8	No signal words required
Skin Sensitization LLNA PMRA 2329903	Negative	No signal words required
Acute Toxicity Studies – Fluopyram Greenhouse Fungicide		
Acute Oral LD_{50} Toxic Class (423) PMRA 1599335	LD_{50} ♀ > 2000 mg/kg	No signal words required
Acute Dermal LD_{50} PMRA 1599336	LD_{50} ♂♀ > 2000 mg/kg	No signal words required
Acute Inhalation LC_{50} PMRA 1599337	LC_{50} ♂♀ > 2.09 mg/L	No signal words required
Primary Eye Irritation PMRA 1599339	MAS[a] = 0/110 MIS[b] = 5.3/110	No signal words required
Primary Skin Irritation PMRA 1599338	MAS[a] = 0/8 MIS[b] = 0/8	No signal words required
Skin Sensitization LLNA PMRA 1599340	Negative	No signal words required

[a] MAS = Maximum Average Score for 24, 48 and 72 hrs
[b] MIS = Maximum Irritation Score

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Fluopyram

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary general population	Rat acute neurotoxicity study	NOAEL = 50 mg/kg bw Reduced motor and locomotor activity	100
	ARfD = 0.5 mg/kg bw		
Repeated dietary	Rat chronic toxicity/carcinogenicity study	NOAEL = 1.2 mg/kg bw/day Numerous effects, primarily in liver, kidney, thyroid and eye	100
	ADI = 0.012 mg/kg bw/day		
Short- and intermediate term dermal[2]	Rat 28 day dermal toxicity study	NOAEL = 300 mg/kg bw/day Clinical chemistry and liver effects	100
Long-term dermal[2]	Rat chronic toxicity/carcinogenicity study	NOAEL = 1.2 mg/kg bw/day Numerous effects, primarily in liver, kidney, thyroid and eye	100
Short- and intermediate-term inhalation[3]	Rat 90 day oral toxicity study	NOAEL = 12.5 mg/kg bw/day Numerous effects	100

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Long-term inhalation[3]	Rat chronic toxicity/carcinogenicity study	NOAEL = 1.2 mg/kg bw/day Numerous effects, primarily in liver, kidney, thyroid and eye	100
Pick-your-own and residential ornamental oral	Rat acute neurotoxicity study	NOAEL = 50 mg/kg bw Reduced motor and locomotor activity	100
Pick-your-own and residential dermal	Rat 28 day dermal toxicity study	NOAEL = 300 mg/kg bw/day Clinical chemistry and liver effects	100
Cancer	Cancer risk (threshold) was addressed through the selected toxicology endpoints		

[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments
[2] Since an oral NOAEL was selected, a dermal absorption factor was used in a route-to-route extrapolation
[3] Since an oral NOAEL was selected, an inhalation absorption factor was used in route-to-route extrapolation.

Table 5 Seed application parameters for Fluopyram ST

Seed	Soybean
Treatment rate:	0.25 mg a.i./seed
Number of seeds/kg	5000.00 seeds/kg
Amount of seeds treated (kg)	1.0 kg
EEC (mg a.i./kg seeds)	1,250.00 mg a.i./kg seeds
Weight of seed	200.00 g/1000 seeds
Seeding rate	111.11 kg seeds/ha
Application rate per ha	138.89 g a.i./ha

Table 6 Toxicity end points for birds and mammals for Fluopyram ST

Study type	Dose-based endpoint	ENTER toxicity dose (mg a.i./kg bw/day)	Uncertainty factor	Value used for the risk assessment
Birds				
Acute oral	LD_{50}	2000	0.1	200.00
Acute dietary	5-d LD_{50}	1642.7	0.1	164.27
Acute oral	NOEL	4.12	N/A	4.12
Mammals				
Acute oral	LD_{50}	2000	0.1	200
Acute oral	NOEL	13.9	N/A	13.90

Table 7 Risk assessment to birds and mammals for Fluopyram ST

Study Endpoint (mg ai/kg bw/day / UF)		EDE (mg ai/kg bw/day)	RQ	Number of seeds needed to reach endpoint	
				min	max
Small bird (0.02 kg)					
Acute	200.00	469.786	2.3	16.00	16.00
Dietary	164.20	469.786	2.9	13.14	13.14
Reproduction	4.12	469.786	114.0	0.33	0.33
Medium bird (0.10 kg)					
Acute	200.00	369.024	1.8	80.00	80.00
Dietary	164.20	369.024	2.2	65.68	65.68
Reproduction	4.12	369.024	89.6	1.65	1.65
Large bird (1.00 kg)					
Acute	200.00	107.584	0.5	800.00	800.00
Dietary	164.20	107.584	0.7	656.80	656.80
Reproduction	4.12	107.584	26.1	16.48	16.48
Small mammals (0.015 kg)					
Acute	200.00	268.470	1.3	12.00	12.00
Reproduction	13.90	268.470	19.3	0.83	0.83
Medium mammals (0.035 kg)					
Acute	200.00	230.885	1.2	28.00	28.00
Reproduction	13.90	230.885	16.6	1.95	1.95
Large mammals (1.00 kg)					
Acute	200.00	127.128	0.6	800.00	800.00
Reproduction	13.90	127.128	9.1	55.60	55.60

Table 8 Fluopyram ST Screening level risk assessment to terrestrial plants

Organism	Exposure	Test substance	Tox value for RQ	Application rates	RQ	Exceed LOC
Vascular plants	seedling emergence	AE C656948 SC 500AG	EC_{25}: 500.00 g a.i./ha	138.89 g a.i./ ha	0.28	No
	vegetative vigour	AE C656948 SC 500AG	EC_{25}: 250.00g a.i./ha	138.89 g a.i./ha	0.56	No

Table 9 Fluopyram ST Risk to aquatic organisms

Organism	Exposure	Test substance	Tox value for RQ (mg a.i./l)	EEC (mg a.i./l)	RQ	Exceedence of LOC
Amphibians	Acute	AE C656948	(LC_{50}/10): 0.178	0.093**	0.52	No
	Chronic	AE C656948	NOAEC: 0.135	0.093**	0.69	No

** 15 cm water depth

Table 10 Risk to terrestrial organisms for FLU + TFS 1:1 SC Fungicide

Organism	Exposure	Test substance	Tox value for RQ	EEC	RQ	Exceedence of LOC
Earthworm (*E. fetida)*	acute	AE C656948 SC 500	LC_{50}(0.5): 207.5 mg a.i./kg dw soil	0.22 mg a.i./kg soil	0.001	No
	Reproduc-tion	AE C656948 SC 500	NOAEC: 11.4 mg a.i./kg dw soil	0.22 mg a.i./kg soil	0.02	No
Honeybees (*A. mellifera* L.)	acute contact	AE C656948 SC 500	LD_{50}: 83.2 µg a.i./ha	0.6 µg a.i./bee[1]	<0.01	No
	Acute oral		LD_{50}: 89 µg a.i./ha	7.25 µg a.i./bee[2]	0.08	No
Predatory mite *(T. pyri)*	acute	AE C656948 SC 500	LR_{50}:>1008 g a.i./ha	403.9 g a.i./ha	<0.4	No
	chronic (reproductio n)	AE C656948 SC 500	NOAEL: 1008 g a.i./ha	403.9 g a.i./ha	0.4	No

[1]contact exposure estimated by multiplying single maximum application rate of 250 g a.i./ha with a factor of 2.4
[2]oral exposure estimated by multiplying single maximum application rate of 250 g a.i./ha with a factor of 29

Table 11 Screening level risk assessment to wild birds for FLU + TFS 1:1 SC Fungicide

Effects	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	200.00	Insectivore (small insects)	20.35	0.10
Reproduction	4.12	Insectivore (small insects)	20.35	4.94
Medium Sized Bird (0.1 kg)				
Acute	200.00	Insectivore (small insects)	15.88	0.08
Reproduction	4.12	Insectivore (small insects)	15.88	3.86
Large Sized Bird (1 kg)				
Acute	200.00	Herbivore (short grass)	16.57	0.08
Reproduction	4.12	Herbivore (short grass)	16.57	4.02

Table 12 Refined risk assessment to wild birds for FLU + TFS 1:1 SC Fungicide

Effects	Toxicity	Food Guild (food item)	Maximum residues				Mean residues			
	mg a.i./kg bw/d		On-field		Off-field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)										
Reproduction	6.8	Insectivore (small insects)	20.35	2.99	1.22	0.18	11.35	1.67	0.68	0.1
	6.8	Granivore (grain and seeds)	5.09	0.75	0.31	0.04	2.43	0.36	0.15	0.02
	6.8	Frugivore (fruit)	10.18	1.5	0.61	0.09	4.85	0.71	0.29	0.04
Medium Sized Bird (0.1 kg)										
Reproduction	6.8	Insectivore (small insects)	15.88	2.34	0.95	0.14	8.86	1.3	0.53	0.08
	6.8	Insectivore (large insects)	3.97	0.58	0.24	0.04	1.89	0.28	0.11	0.02
	6.8	Granivore (grain and seeds)	3.97	0.58	0.24	0.04	1.89	0.28	0.11	0.02
	6.8	Frugivore (fruit)	7.94	1.17	0.48	0.07	3.79	0.56	0.23	0.03
Large Sized Bird (1 kg)										
Reproduction	6.8	Insectivore (small insects)	4.64	0.68	0.28	0.04	2.59	0.38	0.16	0.02
	6.8	Insectivore (large insects)	1.16	0.17	0.07	0.01	0.55	0.08	0.03	0
	6.8	Granivore	1.16	0.17	0.07	0.01	0.55	0.08	0.03	0

Effects	Toxicity mg a.i./kg bw/d	Food Guild (food item)	Maximum residues				Mean residues			
			On-field		Off-field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
		(grain and seeds)								
	6.8	Frugivore (fruit)	2.32	0.34	0.14	0.02	1.11	0.16	0.07	0.01
	6.8	Herbivore (short grass)	16.57	2.44	0.99	0.15	5.89	0.87	0.35	0.05
	6.8	Herbivore (long grass)	10.12	1.49	0.61	0.09	3.3	0.49	0.2	0.03
	6.8	Herbivore (forage crops)	15.33	2.25	0.92	0.14	5.07	0.75	0.3	0.04

Table 13 Screening level risk assessment to mammals for FLU + TFS 1:1 SC Fungicide

Effects	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Mammal (0.015 kg)				
Acute	200.00	Insectivore (small insects)	11.71	0.06
Reproduction	13.90	Insectivore (small insects)	11.71	0.84
Medium Sized Mammal (0.035 kg)				
Acute	200.00	Herbivore (short grass)	36.67	0.18
Reproduction	13.90	Herbivore (short grass)	36.67	2.64
Large Sized Mammal (1 kg)				
Acute	200.00	Herbivore (short grass)	19.60	0.10
Reproduction	13.90	Herbivore (short grass)	19.60	1.41

Table 14 Refined assessmengt of risk to mammals for FLU + TFS 1:1 SC Fungicide

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum residues				Mean residues			
			On-field		Off Field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Mammal (0.015 kg)										
Reproduction	82.4	Insectivore (small insects)	11.71	0.14	0.7	0.01	6.53	0.08	0.39	<0.01

	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum residues				Mean residues			
			On-field		Off Field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
	82.4	Granivore (grain and seeds)	2.93	0.04	0.18	<0.01	1.4	0.02	0.08	<0.01
	82.4	Frugivore (fruit)	5.85	0.07	0.35	<0.01	2.79	0.03	0.17	<0.01
Medium Sized Mammal (0.035 kg)										
Reproduction	82.4	Insectivore (small insects)	10.26	0.12	0.62	0.01	5.72	0.07	0.34	<0.01
	82.4	Insectivore (large insects)	2.57	0.03	0.15	<0.01	1.22	0.01	0.07	<0.01
	82.4	Granivore (grain and seeds)	2.57	0.03	0.15	<0.01	1.22	0.01	0.07	<0.01
	82.4	Frugivore (fruit)	5.13	0.06	0.31	<0.01	2.45	0.03	0.15	<0.01
	82.4	Herbivore (short grass)	36.67	0.45	2.2	0.03	13.02	0.16	0.78	0.01
	82.4	Herbivore (long grass)	22.39	0.27	1.34	0.02	7.31	0.09	0.44	0.01
	82.4	Herbivore (forage crops)	33.93	0.41	2.04	0.02	11.22	0.14	0.67	0.01
Large Sized Mammal (1 kg)										
Reproduction	82.4	Insectivore (small insects)	5.48	0.07	0.33	<0.01	3.06	0.04	0.18	<0.01
	82.4	Insectivore (large insects)	1.37	0.02	0.08	<0.01	0.65	0.01	0.04	<0.01
	82.4	Granivore (grain and seeds)	1.37	0.02	0.08	<0.01	0.65	0.01	0.04	<0.01
	82.4	Frugivore (fruit)	2.74	0.03	0.16	<0.01	1.31	0.02	0.08	<0.01
	82.4	Herbivore (short grass)	19.6	0.24	1.18	0.01	6.96	0.08	0.42	0.01
	82.4	Herbivore (long grass)	11.97	0.15	0.72	0.01	3.91	0.05	0.23	<0.01
	82.4	Herbivore (forage crops)	18.13	0.22	1.09	0.01	5.99	0.07	0.36	<0.01

Table 15 Screening level risk assessment to terrestrial plants for FLU + TFS 1:1 SC Fungicide

Organism	Exposure	Test substance	Tox value for RQ	EEC	RQ	Exceedence of LOC
Vascular plants	seedling emergence	AE C656948 SC 500A G	EC_{25}: 500 g a.i./ha	497.76 g a.i./ ha	**1.00**	yes
	vegetative vigour	AE C656948 SC 500A G	EC_{25}:250 g a.i./ha	403.9 g a.i./ha	**1.62**	yes

Table 16 Refined risk assessment to terrestrial plants for FLU + TFS 1:1 SC Fungicide

	Ground boom (6% drift)
Application rate (250 g a.i./ha)	15.00 g a.i/ha
Seedling emergence	
Cumulative application rate (2 applications with field a DT_{50} of 539 days)	29.87 g a.i./ha
RQ with EC_{25} of 500 g a.i./ha for seedling emergence	0.06 (below LOC)
Risk	no risk
Vegetative vigour	
Cumulative application rate (2 applications with a foliar half-life of 10 days)	24.24 g a.i./ha
RQ with EC_{25} of 250 g a.i./ha for vegetative vigour	0.1 (below LOC)
Risk	no risk

Table 17 Risk to aquatic organisms for FLU + TFS 1:1 SC Fungicide

Organism	Exposure	Test substance	Tox value for RQ (mg a.i./L)	EEC (a.i./L)	RQ
Rainbow trout (*O. mykiss)*	Acute	AEC 656948	(LC_{50}/10): >0.178	0.062*	<0.35
Bluegill sunfish *(L. macrochirus*)	bioaccumulation study	AE C656948	BCF: 18		
Fathead minnow (*P. promelas*)	Chronic: early life stage	AE C656948	NOAEC: 0.135	0.062*	0.46
Sediment dwelling *(C. riparius)* *(C. tetans)*	54 d pore water	AE C656948	NOAEC: 3.8	0.062*	0.16
	54 d sediment	AE C656948	NOAEC: 26.0	0.062*	0.002

Organism	Exposure	Test substance	Tox value for RQ (mg a.i./L)	EEC (a.i./L)	RQ
Amphibians	Acute	AE C656948	(LC_{50}/10): >0.178	0.33**	**<1.85**
	Chronic	AE C656948	NOAEC: 0.135	0.33**	**2.44**
Daphnia *(D. magna)*	Acute	AE C656948	(EC_{50}/2): >8.5	0.062*	<0.017
	Chronic	AE C656948	NOAEC: 1.214	0.062*	0.05
Freshwater green algae (*P.subcapitata)*	Acute	AE C656948 SC 500A G	(EC_{50}/2):1.7	0.062*	0.04
Freshwater diatom *(N. pelliculosa)*	Acute	AE C656948	(EC_{50}/2): 3.1	0.062	0.02
Duckweed (*L. gibba*)	Acute	AE C656948	(EC_{50}/2): 1.3	0.062*	0.05
Sheepshead Minnow (*C. variegatus*)	Acute	AE C656948	(LC_{50}/10): >0.098	0.062*	<0.63
Eastern Oyster (*C. virginica)*	Acute	AE C656948	(LC_{50}/2): 0.22	0.062*	0.28
Saltwater Diatom *(S. costatum)*	Acute	AE C656948	(EC_{50}/2): >0.57	0.062*	<0.11
Marine amphipods (*Leptocheirus plumulosus*)	Acute	AE C656948	(LC_{50}/2): >0.8 (overlying water)	0.062*	<0.08
	Chronic	AE C656948	NOAEC: 0.55 (overlying water)	0.062*	0.11

* 80 cm water depth; ** 15 cm water depth

Table 18 Refined risk assessment to amphibians (Run off) for FLU + TFS 1:1 SC Fungicide

	Exposure	Tox value for RQ (mg a.i./L)	EEC (mg a.i./L)	RQ
Run off	Acute	(LC_{50}/10): >0.178	0.299*	**<1.68**
	Chronic	NOAEC: 0.135	0.261**	**1.93**

* peak concentration; ** 21-day EEC in 15 cm water depth

Table 19 Refined risk assessment to amphibians (Spray drift) for FLU + TFS 1:1 SC Fungicide

	Ground boom (6% drift)
Application rate (250 g a.i./ha)	15.00 g a.i/ha
Cumulative application rate (2 applications, 7 d interval)	29.95 g a.i./ha
EEC	0.02 mg a.i./L*
Acute RQ(LC_{50}:0.178 mg a.i./L)	0.11
Chronic RQ (NOEC:0.135 mg a.i./L)	0.15
Risk	no

*15 cm water depth

Table 20 Registered Alternatives for Fluopyram Greenhouse Fungicide label claims based on mode of action (as of October 2015)

Crop	Target Diseases and Pathogens	Alternative Conventional Active Ingredients (FRAC Mode of Action Group No.)
Greenhouse Cucumber	Grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*)	iprodione (2) ferbam (M3) fenhexamid (17) penthiopyrad (7)
	Powdery mildew (*S. fuliginea*, *E. cichoracearum*)	sulphur (M2) myclobutanil (3) boscalid; pyraclostrobin (7+11) cyprodinil; fludioxonil (9+12) penthiopyrad (7) copper (M1)
Greenhouse pepper	Grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*)	penthiopyrad (7)
	Powdery mildew (*Leveillula taurica*)	sulphur (M2) myclobutanil (3) boscalid; pyraclostrobin (7+11) cyprodinil; fludioxonil (9+12)
Greenhouse Tomato	Grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*)	iprodione (2) ferbam (M3) fenhexamid (17) boscalid; pyraclostrobin (7+11) pyrimethanil (9) cyprodinil; fludioxonil (9+12) penthiopyrad (7)
	Powdery mildew (*Leveillula taurica*)	sulphur (M2) myclobutanil (3)

Crop	Target Diseases and Pathogens	Alternative Conventional Active Ingredients (FRAC Mode of Action Group No.)
		boscalid; pyraclostrobin (7+11) cyprodinil; fludioxonil (9+12)
	Early blight (*Alternaria solani*)	mancozeb (M3) copper (M1) penthiopyrad (7)
	Grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*) - **drip or drench**	n/a
Greenhouse Lettuce	Botrytis rot (*Botrytis cinerea*)	ferbam (M3) fenhexamid (17)

Table 21 List of Supported Uses

Supported Uses on Turf for FLU + TFS 1:1 SC Fungicide	Control of dollar spot (*Sclerotinia homeocarpa*) / turf / 140-200 ml/100m^2, 14-28 days interval/ Apply the FLU + TFS 1:1 SC Fungicide at the first sign of dollar spot symptoms or preventatively when stressful environmental conditions (extended periods of dew >8hrs at temperatures between 13°C-27°C) favour dollar spot development. Under severe disease pressure use the higher rate and shortest interval. / Maximum application of 400 ml/100m^2 product per year.
	Control of brown patch (*Rhizoctonia solani*) / turf / 140-200 ml/100m^2, 14-21 days interval/ Apply the FLU + TFS 1:1 SC Fungicide at the first sign of brown patch symptoms or preventatively when stressful environmental conditions (surface moisture and humidity is greater than 80%, night time temperatures >20^{o}C) favour disease development. Under severe disease pressure use the higher rate and shortest interval. / Maximum application of 400 ml/100m^2 product per year.
	Control of leaf spot (*Bipolaris* spp., *Drechslera* spp.) / turf / 140-200 ml/100m^2, 14-21 days interval/ Apply the FLU + TFS 1:1 SC Fungicide at the first sign of leaf spot symptoms or preventatively when stressful environmental conditions favour disease development. Under severe disease pressure use the higher rate and shortest interval. / Maximum application of 400 ml/100m^2 product per year.
Supported Uses on Soybean for Fluopyram ST	Control of sudden death syndrome (*Fusarium virguliforme*) / Soybeen seed / 0.15 - 0.25 mg ai/seed or 35 to 58 ml / 140,000 soybean seeds.

	FLUOPYRAM ST may be used in combination with other registered Bayer CropScience seed treatment fungicides and insecticides at labelled rates. Tank-mix partners: *FUNGICIDES*: Allegiance FL (metalaxyl), Trilex AL Concentrate (trifloxystrobin, metalaxyl), Trilex AL (trifloxystrobin, metalaxyl), Trilex FS (trifloxystrobin), EverGol Xtend (penflufen, trifloxystrobin), EverGol Energy (penflufen, prothioconazole, metalaxyl). *INSECTICIDES*: Stress Shield 600 (imidacloprid)
Fluopyram Greenhouse Fungicide	Supported Uses on Greenhouse Cucumbers
	Control of grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*) at 500 mL/ha (foliar); 7-10 day intervals; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum two applications per cropping cycle
	Control of powdery mildew (*Sphaerotheca fuliginea*, *Erysiphe cichoracearum*) at 100 mL/ha (foliar); 7-14 day intervals; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum three applications per cropping cycle
	Supported Uses on Greenhouse Peppers
	Control of grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*) at 500 mL/ha (foliar); 7-12 day intervals; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum two applications per cropping cycle
	Control of powdery mildew (*Leveillula taurica*) at 100 mL/ha (foliar); 7-10 day intervals; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum three applications per cropping cycle
	Supported Uses on Greenhouse Tomato
	Control of grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*) at 500 mL/ha (foliar); 10-12 day intervals; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum two applications per cropping cycle
	Control of powdery mildew (*Leveillula taurica*) at 100 mL/ha (foliar); 7-14 day intervals; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum three applications per cropping cycle
	Control of early blight (*Alternaria solani*) at 150-300 mL/ha; thorough coverage of plant foliage; begin fungicide applications preventatively; maximum three applications per cropping cycle

	Control of grey mould on fruit, botrytis leaf blight, and botrytis stem canker (*Botrytis cinerea*) at 40 mL/1000 plants (drip or drench); 7 day intervals from when 9 or more leaves on main shoot are unfolded; apply as drip/drench application; begin fungicide applications preventatively; maximum two applications per cropping cycle; apply required amount in 500 L/ha to 1500 L/ha
	Supported Uses on Greenhouse Lettuce
	Control of botrytis rot (*Botrytis cinerea*) at 500 mL/ha (foliar); minimum 7 day intervals; first application made one week after transplanting, second application can be made up until final head size for harvest is reached; apply required amount in 500 L/ha to 1500 L/ha

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

The seed treatment and greenhouse uses for fluopyram are being reviewed concurrently in Canada and the US. The MRLs proposed for fluopyram in Canada on dry soybeans, tomatoes, peppers, cucumbers and lettuce are the same as corresponding tolerances to be promulgated in the United States. Once established, the American tolerances for fluopyram will be listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide.

Table 1 compares the MRLs proposed for fluopyram in Canada with corresponding American tolerances and Codex MRLs[5]. American tolerances are listed in the Electronic Code of Federal Regulations, 40 CFR Part 180, by pesticide. A listing of established Codex MRLs is available on the Codex Alimentarius Pesticide Residues in Food website, by pesticide or commodity.

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

Food Commodity	Canadian MRL (ppm)	American Tolerance (ppm)	Codex MRL (ppm)
Dry soybeans	0.3	0.04 {0.3}[1]	Not established
Tomatoes	1	Not established yet {1.0}[1]	0.4
Peppers	4	Not established yet {4.0}[1]	Not established
Cucumbers	0.6	Not established yet {0.6}[1]	0.5
Lettuce	40	Not established yet {40}[1]	Not established

[1] The American tolerances in brackets are currently in the process of promulgation.

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

[5] 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
1599748	2008, Fluopyram (AEC 656948) - Technical grade active substance - Discussion of the formation of impurities, DACO: 2.11.4 CBI
1599749	2008, Fluopyram (AEC 656948) - Technical grade active substance - Manufacturing process, DACO: 2.11.1,2.11.2,2.11.3 CBI
2475390	2014, Part 2 report - Fluopyram Technical Fungicide - PART 2 Chemistry requirements for the registration of a technical grade of active ingredient (TGAI)- new manufacturing process, DACO: 2.1,2.2,2.3,2.4,2.5,2.6,2.7,2.8,2.9 CBI
2475391	2014, Fluopyram (AE C656948) - Description of the manufacturing process of the technical grade active substance, DACO: 2.11.1,2.11.2,2.11.3 CBI
2475392	2014, Fluopyram (AE C656948) - Technical grade active substance - Discussion on the formation of impurities, DACO: 2.11.4 CBI
2475397	2014, Fluopyram technical grade active substance - Justification of certified limits for USA and Canada, DACO: 2.12.1 CBI
2475398	2012, Fluopyram (AE C656948) - Determination of technical grade active substance HPLC with external standard, DACO: 2.13.1 CBI
2475401	2013, Validation of AM020212MP1 - Fluopyram (AE C656948) - Determination of technical grade active substance, DACO: 2.13.1 CBI
2475403	2006, Identification of substances by NMR (1H, 13C, 19F, 31P), DACO: 2.13.1,2.13.2 CBI
2475404	2014, Fluopyram (AE C656948) - Impurities in technical grade active substance - HPLC with external standard, DACO: 2.13.1,2.13.2 CBI
2475405	2014, Validation of AM003906MP5 - Fluopyram (AE C656948) - Impurities in technical grade active substance - HPLC with external standard, DACO: 2.13.1 CBI
2475406	2013, Determination of [CBI removed] in fluopyram - IC - external standard, DACO: 2.13.1 CBI
2475408	2013, Determination of [CBI removed] in fluopyram - IC - external standard, DACO: 2.13.1 CBI

2475409	2014, Fluopyram - Determination of [CBI removed] in technical grade active substance GLC-Headspace - external standard, DACO: 2.13.1 CBI
2475410	2014, Validation of GLC-method AM024514MP1 - Fluopyram Determination of [CBI removed] in technical grade active substance – [CBI removed], DACO: 2.13.1 CBI
2475412	2001, [CBI removed], DACO: 2.13.1
2475413	2012, Analytical method – [CBI removed] - Determination of [CBI removed], DACO: 2.13.1
2475414	2014, Material accountability of technical fluopyram (AE C656948), DACO: 2.13.3 CBI
2475474	2014, Fluopyram Technical Fungicide, containing fluopyram, TGAI -WAIVER REQUEST for DACO 2.13.3 BATCH DATA , DACO: 2.13.3 CBI
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2427101	2014, Product Chemistry of FLU+TFS SC 25, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.3.1,3.3.2,3.4.1,3.5.1,3.5.11,3.5.12,3.5.13,3.5.15,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.8,3.5.9,IIIA 1.1,IIIA 1.2.1,IIIA 1.2.3,IIIA 1.3,IIIA 1.4.1,IIIA 1.4.2,IIIA 1.4.3.1,IIIA 1.4.3.3,IIIA 1.4.4,IIIA 1.4.5.1,IIIA 1.5,IIIA 2.1,IIIA 2.11,IIIA 2.12,IIIA 2.14,IIIA 2.2.1,IIIA 2.2.2,IIIA 2.3.1,IIIA 2.3.2,IIIA 2.3.3,IIIA 2.4.1,IIIA 2.5.2,IIIA 2.6.1,IIIA 2.6.2,IIIA 5.2.1,IIIA 5.2.2
2427103	2014, Product Chemistry of FLU+TFS SC 25, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.2.1,3.2.2,3.3.1,3.3.2,3.4.1,3.5.1,3.5.11,3.5.12,3.5.13,3.5.15,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7,3.5.8,3.5.9,IIIA 1.1,IIIA 1.2.1,IIIA 1.2.3,IIIA 1.3,IIIA 1.4.1,IIIA 1.4.2,IIIA 1.4.3.1,IIIA 1.4.3.3,IIIA 1.4.4,IIIA 1.4.5.1,IIIA 1.5,IIIA 2.1,IIIA 2.11,IIIA 2.12,IIIA 2.14,IIIA 2.2.1,IIIA 2.2.2,IIIA 2.3.1,IIIA 2.3.2,IIIA 2.3.3,IIIA 2.4.1,IIIA 2.5.2,IIIA 2.6.1,IIIA 2.6.2,IIIA 5.2.1,IIIA 5.2.2 CBI
2427104	2014, Determination of Physico-Chemical Properties and Storage Stability Test for FLU+TFS SC12.5+12.5 G, DACO: 3.5.10,3.5.14,IIIA 2.13,IIIA 2.7.1 CBI
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2329872	2013, Determination of fluopyram in formulations ; [CBI removed], DACO: 3.4.1
2329873	2013, Validation of [CBI removed] - Determination of fluopyram in formulations - fluopyram FS 600 (600 g/L), DACO: 3.4.1
2329874	2013, Safety-relevant data of fluopyram FS 600 (600 g/L), DACO: 3.5,3.5.11,3.5.12,3.5.8
2329875	2013, Miscibility of fluopyram ST end-use product, DACO: 3.5,3.5.13
2329876	2013, Dielectric breakdown voltage of fluopyram ST end-use product, DACO: 3.5,3.5.15
2329878	2013, Storage stability at elevated temperature and corrosion characteristics of fluopyram FS 600 (600 g/L) - Packaging material: HDPE - Final report (14 days) - Fluopyram FS 600 , DACO: 3.5,3.5.1,3.5.10,3.5.14,3.5.2,3.5.3,3.5.5,3.5.6
2329879	2013, Storage stability at elevated temperature and cold stability of fluopyram FS 600 (600 g/L) - Packaging material: HDPE Final report (8 weeks), DACO: 3.5,3.5.10,3.5.5
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1599280	2008, Product chemistry of fluopyram 500 SC, DACO: 3.3.1,3.3.2,IIIA 1.4.2 CBI
1599283	2008, Manufacturing process description for fluopyram 500 SC, DACO: 3.2.2,IIIA 1.4.5.1 CBI
1599304	2008, Physical, chemical and technical properties of fluopyram SC 500 (500 g/L), DACO: 3.5.1,3.5.2,3.5.3,3.5.6,3.5.7,3.5.9,3.7,8.2.2.1,8.2.3.6,IIIA 2.1,IIIA 2.4.2,IIIA 2.5.1,IIIA 2.5.2,IIIA 2.5.3,IIIA 2.6.1,IIIA 2.8.2,IIIA 2.8.3.1,IIIA 2.8.3.2,IIIA 2.8.5.2,IIIA 2.8.6.1,IIIA 2.8.8.2
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2.0 Human and Animal Health

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2329922	2013, Fluopyram 500 SC - Magnitude of the residue in soybeans, DACO: 7.4.1,7.4.2,7.4.6
2427649	2008, Determination of the residues of AE C656948 in/on tomato drip irrigation of AE C656948 (500 SC) in the greenhouse in Spain, Italy, Germany and Netherlands, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
2427642	2009, Determination of the residues of AE C656948 in/on tomato after dripping in irrigation water of fluopyram SC 500 in the greenhouse in France (South), Netherlands and Spain, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
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2427116	2014, Fluopyram + Trifloxystrobin SC 32.6 (12.5 + 20.1 g/L): Primary Eye Irritation Study in Rabbits, DACO: 4.6.4
2427117	2014, Fluopyram + Trifloxystrobin SC 32.6 (12.5+20.1 g/L): Primary Skin Irritation Study in Rabbits, DACO: 4.6.5
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2329898	2013, Acute oral toxicity up and down procedure in rats - Fluopyram 600 FS, DACO: 4.6.1
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2329902	2013, Primary skin irritation study in rabbits - Fluopyram 600 FS, DACO: 4.6.5

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3.0 Environment

PMRA Doc No	Reference
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1599511	2008, [Phenyl-UL-14C] and [pyridyl-2,6-14C]AE C656948: Aerobic soil metabolism in two US soils, DACO: 8.2.3.4.2
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4.0 Value

PMRA Doc No	Reference
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	10.1, 10.2, 10.2.3.3.
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2427133	2014, Summary of the Efficacy Data and Information for Canada on the Plant Protection Product: Fluopyram + Trifloxystrobin 1:1 Pre-mix Fungicide 25 g a.i./L; containing 12.5 g a.i./L of fluopyram and 12.5 g a.i./L of trifloxystrobin, DACO: 10.1 (OECD),10.3.1 (OECD),12.7,Document M
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2427258	2006, Efficacy of Test Compound 1 on *Botrytis cinerea* and *Sclerotinia* spp. in a springtime greenhouse cultivation of lettuce, DACO: 1.1, 10.2.3.1, 10.2.3.2, 10.2.3.3, 5.2
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