Proposed Registration Decision PRD2015-28

Fluoxastrobin

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Overview

Proposed Registration Decision for Fluoxastrobin

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 Fluoxastrobin Technical Fungicide and Fluoxastrobin ST, containing the technical grade active ingredient fluoxastrobin, as a seed treatment for use on corn.

Fluoxastrobin was previously registered in the end-use products Evito 480 SC Fungicide (registration number 30408) and Disarm 480 SC (registration number 30811). Evito 480 SC Fungicide is a foliar application for control or suppression of certain diseases in wheat, barley, corn, soybean, potato, tomato, peppers and strawberry. Disarm 480 SC is registered to control diseases on turf. For the detailed review see the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide.*

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 Fluoxastrobin Technical Fungicide and Fluoxastrobin ST.

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

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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."

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.

Before making a final registration decision on fluoxastrobin, as a seed treatment for use on corn, 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 fluoxastrobin, which will include the decision, the reasons for it, a summary of comments received on the proposed 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 Fluoxastrobin?

Fluoxastrobin is a conventional fungicide, and the active ingredient in Fluoxastrobin ST, a seed treatment fungicide. Fluoxastrobin works by preventing the germination and growth of susceptible pathogenic fungi. Fluoxastrobin is already registered in Canada, as a foliar fungicide for control or suppression of certain diseases in wheat, barley, corn, soybean, potato, tomato, pepper, strawberry and turf.

Health Considerations

Can Approved Uses of Fluoxastrobin Affect Human Health?

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

Potential exposure to fluoxastrobin may occur through the diet (food and water) or when handling and applying the products. 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.

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

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

In laboratory animals, the technical grade active ingredient fluoxastrobin was of low acute toxicity by the oral, dermal and inhalation routes of exposure. Fluoxastrobin was minimally irritating to the eyes and non-irritating to the skin. Fluoxastrobin did not cause an allergic skin reaction.

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

Short- and long-term (lifetime) animal toxicity tests were assessed for the potential of fluoxastrobin to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. The most sensitive endpoints for risk assessment were effects on the liver and kidneys and on body weight. The risk assessment protects against the findings noted above as well as any other potential effects by ensuring that the level of exposure to humans is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

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

Aggregate dietary intake estimates (food plus water) revealed that the general population and children (1-2 yrs), the subpopulation which would ingest the most fluoxastrobin relative to body weight, are expected to be exposed to less than 63% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluoxastrobin is not of concern for all population sub-groups. There is no evidence that fluoxastrobin is carcinogenic; therefore, a cancer dietary exposure assessment is not required.

Animal studies revealed no acute health concerns. A single dose of fluoxastrobin is not likely to cause acute health effects in the general population (including infants and children). An acute reference dose was not established, therefore an acute dietary intake estimate is not required.

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 at the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout the United States and Canada using fluoxastrobin on corn (field and sweet) are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide***.**

Occupational Risks From Handling Fluoxastrobin ST

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

Seed treatment operators involved in treating field and seed corn seed with Fluoxastrobin ST as well as farmers loading and sowing treated seed can come in direct contact with fluoxastrobin residues on the skin. Therefore, the label specifies that workers treating seed or handling treated seed must wear long pants, a long-sleeved shirt, and shoes plus socks. In addition, workers must wear protective gloves when handling the formulation, treated seed or during clean-out of treatment equipment. The label also requires that closed transfer including closed mixing/loading, calibrating, and closed treatment equipment must be used. Taking into consideration these label statements and the expectation of the exposure period for treaters and planters, health risks to these individuals are not of concern.

Environmental Considerations

What Happens When Fluoxastrobin Is Introduced Into the Environment?

When Fluoxastrobin ST is used according to label directions, it is not expected to pose an unacceptable risk to the environment.

Fluoxastrobin is considered persistent in conditions relevant to the Canadian environment and is expected to carry over to the next growing season. It tends to adsorb to soil and sediment and does not leach appreciably.

Fluoxastrobin ST, when used according to label directions, does not present a risk to small wild mammals, birds, earthworms, bees, beneficial arthropods and other insects, terrestrial plants or aquatic organisms.

Value Considerations

What Is the Value of Fluoxastrobin ST?

Fluoxastrobin ST a seed treatment fungicide will provide growers with a new mode of action to manage three diseases in corn: suppression of seed rot caused by *Aspergillus* spp. and *Penicillium spp.* and seed-borne *Colletotrichum graminicola* which may lead to the suppression of anthracnose stalk rot.

Fluoxastrobin represents a new mode of action to manage *Aspergillus* and *Penicillium* seed rots and anthracnose stalk rot in corn. In addition, suppressing the pathogen responsible for stalk rot may lead to a reduction in corn stalk lodging later in the growing season. The registration of Fluoxastrobin ST will provide growers with a new application method and a seed treatment that may help to manage an aggressive causal pathogen of stalk rot.

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 Fluoxastrobin ST to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with workers coming into direct contact with Fluoxastrobin ST on the skin, workers treating seed or handling treated seed must wear long pants, a long-sleeved shirt, and shoes plus socks. In addition, workers must wear protective gloves when handling the formulation, treated seed or during clean-out of treatment equipment. The label also requires that closed transfer including closed mixing/ loading, calibrating, and closed treatment equipment must be used.

Environment

Fluoxastrobin has the potential to pose a risk to birds when used for corn seed treatment. The product label and the bag of treated seeds require a hazard statement for birds and a precautionary label statement to clean up spilled seeds. A label statement is also required to inform users that fluoxastrobin is inherently toxic to aquatic organisms. Other general environmental label statements are required to reduce potential exposure to the pesticide.

Next Steps

Before making a final registration decision on fluoxastrobin, the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

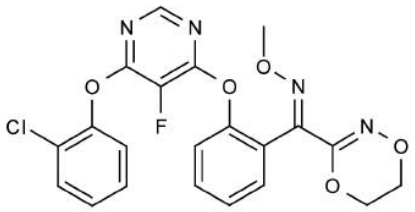
When the PMRA makes its registration decision, it will publish a Registration Decision on fluoxastrobin (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the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

Science Evaluation

Fluoxastrobin

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Fluoxastrobin
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	(*E*)-{2-[6-(2-chlorophenoxy)-5-fluoropyrimidin-4-yloxy] phenyl}(5, 6-dihydro-1, 4, 2-dioxazin-3-yl)methanone *O*-methyloxime
2. Chemical Abstracts Service (CAS)	(1*E*)-[2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy] phenyl](5, 6-dihydro-1, 4, 2-dioxazin-3-yl)methanone O-methyloxime
CAS number	361377-29-9
Molecular formula	$C_{21}H_{16}ClFN_4O_5$
Molecular weight	458.8
Structural formula	
Purity of the active ingredient	95.76%

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

Technical Product—Fluoxastrobin Technical

Property	Result
Colour and physical state	White crystalline solid
Odour	Slight characteristic odour
Melting range	103.1–107.7°C
Boiling point or range	Not applicable

Property	Result
Density	1.4216 g/mL at 25°C
Vapour pressure at 20°C	5.63×10^{-10} Pa
Ultraviolet (UV)-visible spectrum	λ_{max} = 250 nm
Solubility in water	pH: un-buffered, 4, 7, 9 Solubility (mg/L): 2.559, 2.431, 2.292, 2.272
Solubility in organic solvents at 20°C	Solvent: n-heptane, 1-octanol, 2-propanol, xylene, polyethylene glycol, acetone, acetonitrile, dichloromethane, dimethyl sulfoxide, ethyl acetate Solubility (g/L): 0.04, 1.09, 6.7, 38.1, 118.5, >250, >250, >250, >250, >250
n–Octanol-water partition coefficient (K_{ow})	log K_{ow} = 2.86 ± 0.01
Dissociation constant (pK_a)	The active does not dissociate in the pH range of 4 to 9.
Stability (temperature, metal)	Stable at room temperature Stable at 54˚C for two weeks.

End-Use Product—Fluoxastrobin ST

Property	Result
Colour	White
Odour	Musty
Physical state	Suspension
Formulation type	SU (suspension)
Guarantee	480 g/L
Container material and description	HDPE bottle
Density	1.14-1.18 g/mL
pH of 1% dispersion in water	6.8
Oxidizing or reducing action	Neither an oxidizing nor a reducing agent

Property	Result
Storage stability	Stable for 14 days stored in HDPE bottles at 54°C
Corrosion characteristics	No corrosion to HDPE bottles was observed in 14 days at 54°C.
Explodability	Not explosive based on mechanical and thermal tests.

1.3 Directions for Use

To suppress seed rot in corn, caused by *Aspergillus* spp. and *Penicillium* spp., Fluoxastrobin ST is applied at a rate of 1.4-20.8 mL/100 kg seed. For the suppression of seed-borne *Colletotrichum graminicola*, 62.6-125.2 mL/100 kg seed must be applied. The highest rates are to be used when heavy disease pressure is expected

1.4 Mode of Action

Fluoxastrobin is a Group 11 fungicide that interferes with cellular respiration in susceptible pathogenic fungi. It is an inhibitor of spore germination and mycelial growth.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

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

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

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

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for fluoxastrobin was conducted previously and published in the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide*. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes.

The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to fluoxastrobin.

The acute toxicity of the end-use product Fluoxastrobin ST was low via the oral, dermal and inhalation routes in rats. It was non-irritating to the eyes and skin of rabbits. It was not a skin sensitizer in mice using the local lymph node assay.

Results of the toxicology studies conducted on laboratory animals with the end use product Fluoxastrobin ST are summarized in Appendix I, Table 2. The results of toxicology studies conducted on laboratory animals with fluoxastrobin and toxicology endpoints for use in the human health risk assessment are summarized in Appendix I of PRD2012-07, *Fluoxastrobin Technical Fungicide*.

Incident Reports

Since April 26, 2007, registrants have been required by law to report incidents to the PMRA, including adverse effects on Canadian health or the environment. Incidents were searched for the active ingredient fluoxastrobin. No human or domestic animal incidents involving the active ingredient fluoxastrobin have been reported to the PMRA nor did the applicant submit any additional data in relation to this.

3.2 Acute Reference Dose (ARfD)

Refer to the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide*.

3.3 Acceptable Daily Intake (ADI)

Refer to the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide*.

3.4 Occupational Risk Assessment

3.4.1 Toxicological Endpoints

Refer to the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide*.

Occupational exposure to Fluoxastrobin ST is characterized as short- to intermediate-term in duration and is predominantly by the dermal and inhalation routes.

3.4.1.1 Dermal Absorption

Dermal absorption data were not required as dermal risks are based on a dermal endpoint.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to Fluoxastrobin ST during mixing and loading, during treating of seed and during clean-up activities. Exposure to workers treating field and seed corn seed with Fluoxastrobin ST 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 workers treating and applying Fluoxastrobin ST to corn seed, workers bagging, sewing and stacking treated seed and for clean-out personnel. The exposure estimates are based on mixers/loaders/applicators wearing a single layer and gloves for all activities. In addition, exposure estimates for clean-out personnel wearing coveralls over a single layer and gloves were generated.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted. As such, to estimate exposure to commercial workers treating corn seed, unit exposure values for workers wearing a single layer and gloves from a surrogate study were used. For treaters/applicators, the highest mean unit exposures for the active ingredients (those for metalaxyl) were considered appropriate for use in the risk assessment since there was a significant difference between the mean values for the different active ingredients for workers wearing a single layer and gloves. This is considered a conservative approach. Therefore, even though there were only 9 replicates, a mean value was chosen for use in the risk assessment, since the sample size was relatively high and the study was of high quality. For baggers/sewers/stackers, there was not a large difference between the unit exposures calculated for the active ingredients for workers wearing a single layer and gloves. As such, it was considered appropriate to use the combined arithmetic mean for all the replicates for dermal and inhalation exposure in the risk assessment for commercial workers.

For cleaners, the single layer and gloves data are for workers cleaning equipment after corn was treated in the United States. The coveralls and gloves data was for workers cleaning equipment after canola was treated in Canada. The exposure duration for the corn cleaners was approximately 2 hours, and that for the canola cleaners was just over 8 hours. Neither of these scenarios is considered to be representative of all cleaning scenarios. The single layer and gloves scenario is representative of workers cleaning equipment at facilities treating corn, but it is likely that these workers would conduct other activities during the work day since the cleaning only took 2 hours. However, from the study report, it does not appear that these workers were monitored for any other tasks. A risk assessment was conducted with both the corn and the canola cleaner exposure values.

Table 3.4.1 Summary of amount of corn seed handled per day by workers during seed treatment and planting

Crop	Rate (g ai/100 kg seed)	Seed Treated per day (kg)	Amount of Seed Planted per day (kg)
Corn	60	60 000	1350

To estimate exposure to workers treating corn seeds with Fluoxastrobin ST, the study was considered appropriate since workers were monitored while treating canola and corn seeds, and seeds were bagged after treatment. The dust off potential of corn treated with Fluoxastrobin ST was lower than that for corn treated with products used in the surrogate study, as well as for corn treated with two other seed treatment products. As such, the unit exposure data from the study are not expected to underestimate exposure to workers treating corn seed with Fluoxastrobin ST Seed Treatment Fungicide.

For treaters and baggers/sewers/stackers, dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. 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.

For clean-out personnel, unit exposures are normalized for application rate (the highest application rate proposed was used) therefore, dermal exposure was estimated by coupling the unit exposure values with the application rate.

Exposure estimates were compared to the toxicological endpoints (no observed adverse effects levels (NOAEL)) to obtain the margin of exposure (MOE); the target MOE is 100.

Table 3.4.2 summarizes the exposure and risk estimates for fluoxastrobin when workers treat corn seed with Fluoxastrobin ST. Calculated MOEs are above the target MOEs for all workers in commercial seed treatment facilities. All values calculated are representative of closed mixing/loading scenarios. It is expected that the risk to workers using commercial mobile equipment to treat seed would be similar to, or less than, the risk to workers in commercial seed treatment facilities.

Table 3.4.2 Exposure & risk estimates for workers in commercial seed treatment facilities treating corn seeds

Scenario	kg ai handled per day[1]	Unit Exposure		Exposure[2] (mg/kg bw/day)		MOE[3]	
		Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation
Treaters/Baggers		**µg/kg ai handled**					
Treater/Applicator	36.0	2184	6.94	0.983	0.00312	1018	961
Bagger/Sewer/ Stacker	36.0	115.5	8.9	0.0520	0.00401	19240	749
Cleaners		**µg/g ai/100 kg seed**					
Cleanout	60 g	144.3	20.0	0.108	0.015	9240	200

Scenario	kg ai handled per day[1]	Unit Exposure		Exposure [2] (mg/kg bw/day)		MOE [3]	
		Dermal	Inhalation	Dermal	Inhalation	Dermal	Inhalation
Personnel[4] (single layer and gloves for corn)	ai/100 kg seed						
Cleanout Personnel [4] (coveralls and gloves for canola)		56.2	20.0	0.04215	0.015	23725	200

[1] Kg ai handled per day = kg seed treated per day from Table 3.4.1 × application rate (kg ai/kg seed)

[2] For treaters/applicators and baggers/sewers/stackers:

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

[3]Dermal NOAEL = 1000 mg/kg bw/day, target MOE= 100; inhalation NOAEL = 3 mg/kg bw/day, target MOE = 100

[4] For clean-out personnel, unit exposures are normalized for application rate (the highest application rate proposed was used) therefore:

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

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

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

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. 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 (NOAEL) to obtain MOE; the target MOE is 100.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted. Since corn seeds are usually bagged at commercial facilities, a surrogate study conducted with bagged corn seed is considered appropriate to estimate exposure for workers loading and planting treated corn seed.

The dust off potential of corn treated with Fluoxastrobin ST was lower than that for corn treated with the product used in the surrogate study in combination with another seed treatment product. As such, the study is considered adequate to estimate planter exposure from the proposed use on corn. The limitation of using the study as a surrogate to estimate planter exposure is that exposure from planting using an open cab tractor was not assessed.

Table 3.4.3 summarizes the exposure and risk estimates for fluoxastrobin when workers plant corn seed treated with Fluoxastrobin ST. MOEs are well above the target MOEs. Even though closed cabs were used in the study, the calculated MOEs are considered high enough to cover off this uncertainty and closed cab tractors will not be required for planting seed treated with Fluoxastrobin ST.

Table 3.4.3 Exposure & risk estimates for Fluoxastrobin ST for workers planting treated corn from bags

Scenario	Unit exposure (µg/kg ai handled)[1]		kg seed treated per day[2]	App rate (kg ai/kg seed)	kg ai handled per day [3]	Exposure [4] (mg/kg bw/day)		MOE [5]	
	Dermal	Inhalation				Dermal	Inhalation	Dermal	Inhalation
Corn	1515	82.83	1350	0.0006	0.81	0.0153	0.000839	65200	3580

[1] Unit exposure values for planters of treated corn seed are from a surrogate planting exposure study
[2] Data from Table 3.4.1
[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] Dermal NOAEL = 1000 mg/kg bw/day, target MOE= 100; inhalation NOAEL = 3 mg/kg bw/day, target MOE = 100

3.4.3 Residential Exposure and Risk Assessment

Bystander exposure should be negligible since the potential for drift is expected to be minimal when planting treated seeds.

3.5 Food Residues Exposure Assessment

The Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide* provides a summary of data reviewed and the rationale for the regulatory decision. No new data were submitted with the current petition. Previously reviewed data, summarized in PRD2012-07, *Fluoxastrobin Technical Fungicide*, were used to support the seed treatment use of fluoxastrobin in/on corn (field and seed). Refer to the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide* for further details.

3.5.1 Concentrations in Drinking Water

Concentrations in drinking water as a result of seed treatment uses are expected to be less than those resulting from the registered use of fluoxastrobin as a foliar spray. Refer to the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide* for more details on drinking water concentrations of fluoxastrobin residues as a result of foliar application.

3.5.2 Residues in Plant and Animal Foodstuffs

Refer to the Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide*.

3.5.3 Dietary Risk Assessment

A chronic (non-cancer) dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.16), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.3.1 Chronic Dietary Exposure Results and Characterization

For the chronic dietary exposure assessment, MRL-level residues were used for all domestic and imported crops and livestock commodities. It was assumed that 100% of the crops were treated. The basic chronic dietary exposure from all supported fluoxastrobin food uses (alone) for the total population, including infants and children, and all representative population subgroups is 20.5% of the acceptable daily intake. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to fluoxastrobin from food and water is 27.1% (0.004066 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children of 1-2 yrs old at 62.6% (0.009391 mg/kg bw/day) of the ADI.

3.5.3.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore, no acute dietary exposure assessment was conducted.

3.5.4 Aggregate Exposure and Risk

The aggregate risk for fluoxastrobin consists of exposure from food and drinking water sources only as there are no residential uses considered for this petition.

3.5.5 Maximum Residue Limits

The fluoxastrobin MRLs captured in Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide* and regulated under the *Pest Control Products Act* may be found on Health Canada's MRL Database.

4.0 Impact on the Environment

Refer to PRD2012-07, *Fluoxastrobin Technical Fungicide* for a detailed assessment of the environmental impacts of fluoxastrobin.

Environmental 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 June 8 2015, no environmental incident reports involving Fluxastrobin had been submitted to the PMRA.

4.1 Fate and Behaviour in the Environment

The properties and environmental fate characterization of fluoxastrobin have been previously reviewed and reported in PRD2012-07, *Fluoxastrobin Technical Fungicide*.

4.2 Environmental Risk Characterization

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

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints.

Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

The effects of fluoxastrobin residues on terrestrial organisms have been previously reviewed and reported in PRD2012-07, *Fluoxastrobin Technical Fungicide*. However, a new risk assessment was conducted to determine whether seeds treated at the maximum proposed application rate of 125.2 mL/100 kg seed (60.1 g a.i./100 kg seed) could present an unacceptable risk to birds and small mammals.

The estimated exposure of birds and mammals to fluoxastrobin through the consumption of treated seeds is presented in Appendix I, Table 3, and the toxicity endpoints for birds and small mammals are presented in Appendix I, Table 4.

The screening level risk assessment for birds is conducted with data from acute single dose toxicity studies, and reproduction studies. Data from avian short-term dietary studies can be used if further characterization of the acute risk is required. The screening risk assessment for small mammals is conducted with data from oral acute studies and ecologically relevant long term studies.

For birds, no mortalities or signs of intoxications were observed in any of the dosed animals in the acute or dietary studies, and the screening level risk quotients based on avian oral acute endpoints do not exceed the level of concern (Appendix I, Table 5).

The most sensitive reproduction endpoint was observed in the study with the mallard duck (PMRA document number 1692344). In this study, the female body weights, the number of eggs laid/hen, and the number of eggs set/hen were all statistically reduced in the group dosed with 188 mg a.i./kg bw/day as compared with the control group. The lowest dose at which no adverse concentrations were observed (NOAEL) was determined to be 53 mg a.i./kg bw/day. The screening level risk quotients calculated with this NOAEL exceed the level of concern for small and medium-sized birds.

The availability of seeds in the field is expected to be affected by factors such as the seeding rate (the number of seeds per unit area), whether planted seeds are buried or exposed, and whether seeds are spilled. It is estimated that small and medium-sized birds would reach the reproduction NOAEL if they respectively ingested approximately 5 or 23 treated seed kernels. When corn is planted in spring, a little more than 3% of the seeds typically remain unburied on the soil surface and would be available to foraging birds. Assuming a typical planting density for corn, small and medium birds would have to forage and consume all of the unburied seeds on a 17 or an 83 square metre area, respectively, to be exposed to the NOAEL dose. These areas are relatively large for a small or medium-sized bird to cover during feeding. The potential risk was further characterised by calculating the risk quotients from the lowest concentration that led to adverse effects.

Using this LOAEL (188 mg a.i./kg bw/day) instead of the NOAEL, the RQs for small and medium birds fall below the level of concern (RQ = respectively 0.81 and 0.64). Small and medium birds would have to respectively eat 17 and 83 seeds, on areas of 59 and 295 square meters to reach the LOAEL (Appendix I, Table 5).

The effects on body weight and egg production observed in birds in the reproductive test are expected to have resulted from chronic exposure to the active ingredient. Given that only a relatively small amount of seeds is expected to be available on the soil surface before seeds start germinating, the risk associated with the proposed use of fluoxastrobin is expected to be minimal.

In order to reduce the possibility that birds could consume larger quantities of treated seed, the product label and the bag of treated seeds require a hazard statement for birds and a precautionary label statement to clean up spilled seeds.

For small mammals, the screening level risk quotients were below the level of concern for the identified most sensitive environmentally relevant endpoints, and the risk to small mammals associated with the proposed seed treatment is estimated to be low (Appendix I, Table 5).

Please refer to the PMRA Proposed Registration Decision, PRD2012-07, *Fluoxastrobin Technical Fungicide* for the environmental risk assessment of fluoxastrobin on organisms other than birds and mammals.

4.2.2 Risks to Aquatic Organisms

Refer to PRD2012-07, *Fluoxastrobin Technical Fungicide*.

5.0 Value

5.1 Consideration of Benefits

The registration of Fluoxastrobin ST will provide growers with a new mode of action to suppress *Aspergillus* and *Penicillium* seed rots and seed-borne *Colletotrichum graminicola*. Alternatives for these uses do exist, however they are both from the same fungicide group (Group 3).

Fluoxastrobin ST could be part of an integrated pest management program, which incorporates other management practices such as treatment of field corn varieties that would be tolerant to the labeled diseases.

Group 11 fungicides are considered to pose a high risk for resistance development. However given that Fluoxastrobin ST will be applied in a single application and that relatively small amounts will be applied, the risk of resistance development for this product is considered low.

5.2 Effectiveness Against Pests

Results from seed bioassay trials were submitted which supported the claims for seed rot caused by *Aspergillus* spp. and *Penicillium* spp..

Results from four greenhouse trials demonstrated the potential efficacy of fluoxastrobin against the fungal pathogen, *C. graminicola*. Due to the timing and methodology of the disease assessments, the evidence to support the stalk rot claim was considered to be indirect. However the weight of evidence supported a claim of suppression of seed borne *Colletotrichum graminicola*, and application at the highest labelled rate may lead to the suppression of anthracnose stalk rot caused by seed borne *C. graminicola* later in the growing season.

5.3 Non-Safety Adverse Effects

No adverse effects were noted when Fluoxastrobin ST was applied at rates up to 188 ml/100 kg seed.

5.4 Supported Uses

The claim of Fluoxastrobin ST for control of seed rot (*Aspergillus* spp. and *Penicillium* spp.) in corn, when used according to label directions, is supported. The claim of suppression of seed-borne *Colletotrichum graminicola*, which may lead to the suppression of anthracnose stalk rot later in the growing season, is also supported.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

Refer to PRD2012-07, *Fluoxastrobin Technical Fungicide*.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants, and contaminants in the end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[5] The list is used as described in the PMRA Notice of Intent NOI2005-01[6] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02,[7] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

Fluoxastrobin ST, the end-use product being proposed for registration has, as a component, the preservative 1, 2-benzisothiazoline-3-one, which contains low levels of polychlorinated dibenzodioxins and furans (TSMP Track 1). As the use of this preservative in pest control products at a maximum of 0.1% was reassessed by the PMRA in 2012 and found to be acceptable because dioxin and furan levels are low/being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of TSMP, at this time no further action is required.

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5 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

6 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

7 DIR2006-02, *Formulants Policy and Implementation Guidance Document*.

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

7.0 Summary

7.1 Human Health and Safety

Workers treating field and seed corn seed with Fluoxastrobin ST and workers handling corn seed treated with Fluoxastrobin ST are not expected to be exposed to levels of Fluoxastrobin ST that will result in health risks of concern when Fluoxastrobin ST is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

7.2 Environmental Risk

Fluoxastrobin ST, when used according to label directions, does not present a risk to small wild mammals, earthworms, bees, beneficial arthropods and other insects, terrestrial plants or aquatic organisms. To mitigate any potential risk to birds, a precautionary label statement to clean up spilled seeds is required.

7.3 Value

Fluoxastrobin ST will provide growers with a new mode of action to manage three diseases in corn: suppression of seed rot caused by *Aspergillus* spp. and *Penicillium* spp. and seed-borne *Colletotrichum graminicola*, which may lead to the suppression of anthracnose stalk rot.

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 Fluoxastrobin Technical Fungicide and Fluoxastrobin ST, containing the technical grade active ingredient fluoxastrobin, as a seed treatment for use on corn.

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

°C	degrees Centigrade
µg	micrograms
a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
CAS	Chemical Abstracts Service
dw	dry weight
EDE	estimated daily exposure
EEC	estimated exposure concentration
FDA	*Food and Drugs Act*
FIR	food ingestion rate
g	gram
ha	hectare(s)
HDPE	high density polyethylene
HPLC-MS/MS	high-performance liquid chromatography methods with tandem mass spectrometry
HPLC-UV	high performance liquid chromatography with ultraviolet detection
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LC-MS/MS	Liquid Chromatography with tandem Mass Spectrometry
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOQ	limit of quantitation
mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NZW	New Zealand white
Pa	Pascals
PCPA	*Pest Control Product Act*
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PRD	proposed registration decision
RQ	risk quotient
spp.	species

TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
UV	ultraviolet

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Soil/sediment	none	HEC 5725	LC-MS/MS (m/z: 459, 427)	5.0 µg/kg		1692411, 1692415
	none	HEC 5725-Z-isomer	LC-MS/MS (m/z: 459, 427)	5.0 µg/kg		1692411, 1692415
	none	HEC 5725-E-des-chlorophenyl	LC-MS/MS (m/z: 347, 230)	5.0 µg/kg		1692411, 1692415
	none	HEC 5725-E-Carboxylic acid	LC-MS/MS (m/z: 418, 342)	5.0 µg/kg		1692411, 1692415
Water	none	HEC 5725	HPLC-MS/MS (m/z : 458.8, 426.9)	0.05 µg/L	Surface water	1692423
	none	HEC 5725	HPLC-UV	2 µg/L	Toxicity test water	1692428
	none	HEC 5725-E-des-chlorophenyl	HPLC-UV	2 µg/L	Toxicity test water	1692428
	none	HEC 5725-E-Carboxylic acid	HPLC-UV	0.1 mg/L	Toxicity test water	1932516

Table 2 Toxicity Profile of Fluoxastrobin ST Containing Compound Fluoxastrobin

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

Study Type/Animal/PMRA Documents Number	Study Results
Acute oral toxicity Sprague-Dawley rats 2493874	LD_{50} > 5000 mg/kg bw ♀ Low toxicity
Acute dermal toxicity Sprague-Dawley rats 2493879	LD_{50} > 5000 mg/kg bw Low toxicity
Acute inhalation toxicity (nose-only) Sprague-Dawley rats 2493876	LC_{50} > 5.15 mg/L Low toxicity

Study Type/Animal/PMRA Documents Number	Study Results
Dermal irritation NZW rabbits 2493878	MAS = 0 Non-irritating
Eye irritation NZW rabbits 2493877	MAS = 0 Non-irritating
Dermal sensitization LLNA CBA/J mice 2493879	Non-sensitizer

Table 3 Estimated exposure to generic birds and mammals through the consumption of seed treated with fluoxastrobin

Crop	# seeds/ g seed	Generic body weight of organism (kg)	FIR [a] (g dw diet/day)	Estimated exposure [b] (# seeds/day)
Field corn (including corn grown for seed)	2.63	**Birds**		
		0.02	5.08	13
		0.1	19.9	52
		1	58.1	153
		Mammals		
		0.015	2.18	6
		0.035	4.37	12
		1	68.7	181

[a] Food Ingestion Rate is based on equations from Nagy (1987):
For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used:
FIR (g dry weight/day) = $0.398(\text{bw in g})^{0.850}$
For generic birds with body weight greater than 200 g, the "all birds" equation was used:
FIR (g dry weight/day) = $0.648(\text{bw in g})^{0.651}$
For mammals, the "all mammals" equation was used:
FIR (g dry weight/day) = $0.235(\text{bw in g})^{0.822}$
Food ingestion is calculated in terms of g dry weight of food per day. As a conservative estimate, treated seed is assumed to be equivalent to dry weight of food as minimal moisture is expected to be present in treated seeds ready for planting.

[b] Estimated exposure calculated as # seeds/g × FIR. Assumes that 100% of the diet is comprised of treated seeds.

Table 4 Toxicity fluoxastrobin to birds and mammals expressed as a daily dose

Organism	Exposure (study PMRA#)	Test substance	Endpoint value[a]	Most sensitive endpoint applying uncertainty factor[b]
Birds				
Bobwhite quail	Acute (1692312)	fluoxastrobin technical	LD_{50} >2000 mg a.i./kg bw (no mortality at highest dose)	LD_{50} × 0.1: 200 mg a.i./kg bw
Bobwhite quail	5d-Dietary (1692322)	fluoxastrobin technical	LD_{50} >939 mg a.i./kg bw/day (no mortality at highest dose)	LD_{50} × 0.1: 94 mg a.i./kg bw/day
Mallard duck	5d-Dietary (1692328)	fluoxastrobin technical	LD_{50} > 2195 mg a.i./kg bw/day (no mortality at highest dose)	
Bobwhite quail	22 weeks-Reproduction (1692336)	fluoxastrobin technical	NOEL: 82 mg a.i./kg bw/day (no adverse effects observed in any of the control or treatment groups)	NOEL: 53 mg a.i./kg bw/day (female bw; egg production)
Mallard duck	21 weeks – Reproduction (1692344)	fluoxastrobin technical	NOEL: 53 mg a.i./kg bw/day (female bw; egg production)	
Mammals				
Rat	Acute (1692408)		LD_{50} >2000 mg a.i./kg bw (no mortality at highest dose)	LD_{50} × 0.1: 200 mg a.i./kg bw
Rat	2-generation dietary reproductive toxicity (diet) (1692523)		NOAEL = 741.6 mg/kg bw/day (No reproductive toxicity observed at highest dose tested)	NOAEL = 741.6 mg/kg bw/day

[a] Endpoints reported as a concentration are converted to a daily dose: Toxicity Dose = Concentration × (FIR/bw). FIR and bw are drawn from original studies. No conversion required for acute oral endpoints due to the nature of the test (already a dose). Mammal endpoints typically reported as doses by study authors; mammal doses were reported in original fluoxastrobin review (PRD2012-07, *Fluoxastrobin Technical Fungicide*).

[b] The most conservative endpoint for each study type for birds and mammals was used for the risk assessment. In addition, the acute endpoints were divided by an uncertainty factor of 10 to account for potential differences in species sensitivity as well as varying protection levels (population, community, individual).

Table 5 Screening level risk quotients

	Study Endpoint (mg ai/kg bw/day × UF)	EDE[a] (mg ai/kg bw/day)	RQ[b]
Small bird (0.02 kg)			
Acute	200	153	0.8
Reproduction	53	153	2.9
Medium bird (0.10 kg)			
Acute	200	120	0.6
Reproduction	53	120	2.3
Large bird (1 kg)			
Acute	200	35	0.2
Reproduction	53	35	0.7
Small mammals (0.015 kg)			
Acute	200	87	0.4
Reproduction	741.6	87	0.1
Medium mammals (0.035 kg)			
Acute	200	75	0.4
Reproduction	741.6	75	0.1
Large mammals (1 kg)			
Acute	200	41	0.2
Reproduction	741.6	41	0.06

[a]Estimated daily exposure; is calculated using the following formula: (FIR/bw) × EEC, where FIR= food ingestion rate, bw = body weight, EEC = estimated environmental concentration.

The FIR was estimated according to equations by Nagy, 1987. Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = 0.398(bw in g)$^{0.850}$; All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(bw in g)$^{0.651}$. All mammals equation: FIR (g dry weight/day) = 0.235(bw in g)$^{0.822}$. EEC= concentration of the active ingredient per Kg seed.

[b]Risk quotient (RQ) = exposure/toxicity. Shaded cells indicate that the RQ exceeds the level of concern (LOC =1).

Table 6 Further characterization of the avian reproductive risk

Endpoint	Generic body weight of bird (kg)	Number of seeds to reach endpoint	Required feeding area to reach endpoint (m^2)	
			Assuming that 100% of seeds are available for consumption [b]	Assuming that 3.3% of seeds are available for consumption [c]
NOAEL: 53 mg ai/kg bw/day	0.02	4.6	0.54	17
	0.1	23.2	2.7	83
LOAEL: 188 mg ai/kg bw/day	0.02	16.5	1.9	59.1
	0.1	82.3	9.7	295.4

[a] Number of seeds to reach endpoint calculated as Daily dose (mg a.i./kg bw or mg a.i./kg bw/day) × generic body weight of organism (kg) ÷ Amount of active ingredient per seed (mg a.i./seed). For daily doses refer to Table 4. Amount of active ingredient per seed for corn is 0.23 mg a.i./seed: Proposed rate of application (60.1g a.i./100 kg seed) ÷ 263 158 seeds per 100 kg seed × 1000.

[b] Calculated by dividing the number of seeds to reach the endpoint with the seeding rate expressed as the number

of seeds/m^2. For corn, it is assumed that the seeding rate is 32 kg seeds/ha which results in 8.48 seeds/m^2 assuming a density of 2650 seeds/kg seed.

[c] De Snoo and Luttik (2004) report that the proportion of seeds available for consumption following planting (i.e., still exposed) will be 0.5% for precision drilling, 3.3% for standard drilling in the spring and 9.2% for standard drilling in autumn. As corn seeds are planted in the spring, it was considered that 3.3% of seeds would be available for consumption (resulting in 0.28 available seeds/m^2). Even distribution was assumed.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
1742079	2003, Product Chemistry - Fluoxastrobin Technical, DACO: 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12.1, 2.13.1, 2.13.2 , 2.13.3, 2.13.4 CBI
1692311	2001, Physical and Chemical Properties of HEC 5725 - a.i., DACO: 2.14.1, 2.14.10, 2.14.11, 2.14.2, 2.14.3, 2.14.4, 2.14.6, 2.14.7, 2.14.8, 2.14.9 CBI
1692321	1999, Spectral Data Set of HEC 5725 - a.i., DACO: 2.14.12 CBI
1692360	1999, Determination of safety-relevant data of HEC 5725, DACO: 2.16 CBI
1692381	2001, Storage Stability Data of HEC 5725 Technical, DACO: 2.14.14 CBI
1692397	2000, Thermal Stability of the Active Ingredient HEC 5725 Technical, DACO: 2.14.13 CBI
1692547	2008, Product Chemistry - Fluoxastrobin Technical, DACO: 2.1, 2.10, 2.3, 2.3.1, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9
1932511	2001, Determination of impurities in technical grade active ingredient. Assay -- HPLC -- external standard, DACO: 2.3.1 CBI
1932512	2003, Fluoxastrobin byproducts -- HPLS -- external standard, DACO: 2.3.1 CBI
1932513	2010, Fluoxastrobin (HEC 5725) -- Statement to the Validation of Analytical Methods -- AM000303MP1 & 2005-0011901-01, DACO: 2.3.1 CBI
1932514	2001, Validation of HPLC-method 2005-0011901-01 -- By-products of HEC 5725 Technical, HPLC -- external standard, DACO: 2.3.1 CBI
1932515	2006, Validation of HPLC-method AM000303MP1 -- Fluoxastrobin byproducts HPLC external standard, DACO: 2.3.1 CBI
1692411	2001, Residue analytical Method 00611 (MR-645/99) for the determination of HEC 5725-E-isomer, HEC 5725-Z-isomer, HEC 5725-E-des-chlorphenyl and HEC 5725-E/Z-carboxylic acid in soil by HPLC-MS/MS, DACO: 8.2.2.1
1692415	2002, Independent laboratory validation of Bayer Method 00611: residue analytical method for the determination of HEC 5725-E-isomer, HEC 5725-Z-isomer, HEC 5725-E-des-chlorphenyl and HEC 5725-E/Z-carboxylic acid in soil by HPLC-MS/MS, DACO: 8.2.2.1
1692418	2002, Aerobic degradation and metabolism of [CBI removed]HEC5725 in water/sediment system, DACO: 8.2.2.2,8.2.3.5.2,8.2.3.5.4
1692419	2001, Enforcement Method 00705 for the determination of residues of HEC 5725-E-isomer and HEC 5725-Z-isomer in soil by HPLC-MS/MS, DACO: 8.2.2.1
1692423	2001, Enforcement method for the determination of HEC 5725 in drinking water and surface water by HPLC-MS/MS, DACO: 8.2.2.3
1692428	1999, Method for the determination of HEC 5725 and HEC 7155 in test water from aquatic toxicity tests by HPLC, DACO: 8.2.2.3

PMRA Document Number	Reference
1932516	2001, Method for Determination of HEC 5725-carboxylic acid in Test Water from Aquatic Toxicity Tests by HPLC, DACO: 8.2.2 CBI
1932517	2010, Waiver Request for Requirement to Provide Validated Method for Fluoxastrobin and Its Degradates in Sediment, DACO: 8.2.2
1932518	2010, Waiver Request for Requirement to Perform Method Validation for Fluoxastrobin in Drinking Water, DACO: 8.2.2
2361993	2013, Certification of code names - Fluoxastrobin ST, DACO: 3.1 CBI
2361994	2013, Description of materials used to produce fluoxastrobin ST end use product, DACO: 3.2.1 CBI
2361996	2013, Description of the formulation process for fluoxastrobin ST end use product, DACO: 3.2.2, 3.5.4 CBI
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2362001	2013, Physical, chemical and technical properties of fluoxastrobin FS 480 (480 g/L), DACO: 3.5.1, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.9 CBI
2362002	2013, Storage stability at elevated temperature and corrosion characteristics of fluoxastrobin FS 480 (480 g/L) - Packaging material: HDPE - Final report (14 days), DACO: 3.5.10, 3.5.14, 3.5.5 CBI
2362003	2013, Miscibility of fluoxastrobin ST end-use product, DACO: 3.5.13 CBI
2362004	2013, Dielectric breakdown voltage of fluoxastrobin ST end-use product, DACO: 3.5.15 CBI
2362005	2013, Safety-relevant data of fluoxastrobin FS 480 (480 g/L), DACO: 3.5.11, 3.5.12, 3.5.8 CBI

2.0 Human and Animal Health

PMRA Document Number	Reference
1885209	2010, Observational Study to Determine Dermal and Inhalation Exposure to Workers in Commercial Seed Treatment Facilities: Mixing/Treating with a Liquid Pesticide Product and Equipment Clean-out. DACO: 5.10, 5.11,5.4, 5.5, 5.6, 5.7, 5.9, 7.3.3, 7.5.4

1965962.	2008, Determination of Operator Exposure to Imidacloprid During Loading/Sowing of Gaucho Treated Maize Seeds Under Realistic Field Conditions in Germany and Italy. DACO: 5.6
2362022	2013, Occupational Exposure and Risk Assessment for Fluoxastrobin Based Suspension Concentrate Seed Treatment Formulation for Corn Seed Use in Canada. DACO: 5.1, 5.15, 5.2, 5.3
2362007	2013, Acute oral toxicity up and down procedure in rats - Fluoxastrobin FS 480, DACO: 4.6.1
2362009	2013, Acute dermal toxicity study in rats - Fluoxastrobin FS 480, DACO: 4.6.2
2362011	2013, Acute inhalation toxicity study in rats - Fluoxastrobin FS 480, DACO: 4.6.3
2362013	2013, Primary eye irritation study in rabbits - Fluoxastrobin FS 480, DACO: 4.6.4
2362015	2013, Primary skin irritation study in rabbits - Fluoxastrobin FS 480, DACO: 4.6.5
2362019	2013, Local lymph node assay (LLNA) in mice - Fluoxastrobin FS 480, DACO: 4.6.6

3.0 Environment

PMRA Document Number	Reference
1692312	2000, HEC 5725 Technical a.i.: Acute Oral Toxicity for Bobwhite Quail, Data Numbering Code: 9.6.2.1
1692322	2001, HEC 5725 Technical: 5-day Dietary LC_{50} for Bobwhite Quail (*Colinus virginianus*), Data Numbering Code: 9.6.2.4
1692328	2001, HEC 5725 Technical: 5-day Dietary LC_{50} to Mallard Duck (*Anas platyrhynchos*), Data Numbering Code: 9.6.2.5
1692336	2001, Reproduction Study in Bobwhite Quail with HEC 5725 Technical: (by Dietary Admixture), Data Numbering Code: 9.6.3.1
1692344	2003, Effect of Technical HEC 5725 on Mallard Reproduction, Data Numbering Code: 9.6.3.2
1692408	1996, HEC 5725 Study for Acute Oral Toxicity in Rats, Data Numbering Code: 9.7.1
1692523	2004, A Two-Generation Reproductive Toxicity Study with HEC 5725 in the Wistar Rat, Data Numbering Code: 9.7.1

4.0 Value

PMRA Document Number	Reference
2361983	2013, Fluoxastrobin ST Seed Treatment Fungicide for control of seed rot / preemergence damping-off of corn caused by *Aspergillus* spp. and *Penicillium* spp., DACO: 10.1, 10.2.2, 10.2.3.1, 10.2.3.3
2361986	2013, Fluoxastrobin ST Seed Treatment Fungicide for suppression of Anthracnose Stalk Rot (*Colletotrichum graminicola*) in corn - Part 10 efficacy/value, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.3, 10.3.1, 10.3.2, 10.4, 10.5

B. ADDITIONAL INFORMATION CONSIDERED

i) Published Information

1.0 Environment

Nagy, K.A., 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs 57:111-128.

de Snoo, G.R., R. Luttik, 2004. Availability of pesticide-treated seed on arable fields. Pest Management Science 60:501-506.