Proposed Registration Decision PRD2012-07

Fluoxastrobin Technical Fungicide

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Table of Contents

Overview

Proposed Registration Decision for Fluoxastrobin Technical Fungicide

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 Evito 480 SC Fungicide, containing the technical grade active ingredient fluoxastrobin, to control or suppress certain diseases in wheat, barley, corn (field, seed and sweet), soybean, potato, tomato, pepper, strawberry and turf. In addition, an import maximum residue level (MRL) on celery is being granted.

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 section provides detailed technical information on the human health, environmental and value assessments of Fluoxastrobin Technical Fungicide and Evito 480 SC Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* (PCPA) 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 (example, children) as well as organisms in the environment (example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more

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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."

information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on fluoxastrobin, the PMRA will consider all 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 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 section of this consultation document.

What Is Fluoxastrobin?

Fluoxastrobin is the fungicidal active ingredient in Evito 480 SC Fungicide. Evito 480 SC Fungicide is a foliar applied, translaminar, systemic fungicide with preventative activity against diseases on wheat, barley, corn, soybean, potato, tomato, pepper, strawberry, and turf. It acts on pathogen cells by inhibiting fungal respiration, which in turn inhibits spore germination, spore penetration and fungal growth.

Health Considerations

Can Approved Uses of Fluoxastrobin Affect Human Health?

Fluoxastrobin is 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 product 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 (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 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 allergic skin reactions. Consequently, no hazard signal words are required on the label.

The acute toxicity of the end-use product Evito 480 SC Fungicide, containing fluoxastrobin, was low via oral, dermal and inhalation routes. Evito 480 SC Fungicide was non-irritating to the eyes and slightly irritating to the skin. Evito 480 SC Fungicide did cause allergic skin reactions in laboratory animals. Consequently, the hazard signal words "Potential Skin Sensitizer" are required on the product label.

Health effects in animals given repeated doses of fluoxastrobin included effects on the liver, kidneys, urinary system and blood calcium levels. Fluoxastrobin did not damage genetic material or cause cancer at doses that were relevant to human risk assessment. There was no indication that fluoxastrobin caused damage to the nervous system or immune system. Fluoxastrobin did not cause birth defects in animals and there were no effects on the ability to reproduce.

When fluoxastrobin was given to pregnant or nursing animals effects on the developing fetus and juvenile animal were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to fluoxastrobin than the adult animal.

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

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children (1-2 years old), the subpopulation which would ingest the most fluoxastrobin relative to body weight, are expected to be exposed to less than 46% 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 was 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 was not required.

The *Food and Drugs Act (FDA)* 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 FDA purposes through the evaluation of scientific data under the PCPA. 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), wheat, barley, soybean, potato, tomato, pepper, strawberry and celery are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Consultation Document.

Risks in Residential and Other Non-Occupational Environments are Not of Concern

Individuals may come into contact with Evito 480 SC Fungicide when contacting commercially treated turf or picking strawberries at pick-your-own operations. Risks to these individuals are not of concern when label directions are followed.

Occupational Risks From Handling Evito 480 SC Fungicide

Occupational risks are not of concern when Evito 480 SC Fungicide is used according to the proposed label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Evito 480 SC Fungicide, as well as field workers, re-entering freshly treated fields can come in direct contact with fluoxastrobin residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying Evito 480 SC Fungicide must wear a long-sleeved shirt, long pants, shoes plus socks, and chemical resistant gloves. The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, risks to these individuals are not a concern.

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.

Environmental Considerations

What Happens When Fluoxastrobin Is Introduced Into the Environment?

When fluoxastrobin is applied as a fungicide on turf and field crops, it can find its way into soil and water. Fluoxastrobin tends to adsorb to soil and sediment and does not leach appreciably. It is considered persistent in conditions relevant to the Canadian environment and is expected to carry-over to the next growing season.

Fluoxastrobin presents negligible risks to terrestrial plants, earthworm, bees, birds and small mammals, at the proposed use rates. Studies conducted on artificial substrates, however, suggest that fluoxastrobin could pose a risk to beneficial predatory and parasitic arthropods. Fluoxastrobin could also pose a risk to freshwater algae, invertebrates, fish and amphibians; and to marine algae and invertebrates. In order to minimize the potential for exposure resulting from off-field drift, no-spray buffer zones will be required between the treated area and downwind aquatic habitats.

Value Considerations

What Is the Value of Evito 480 SC Fungicide?

Fluoxastrobin is a preventative fungicidal active ingredient effective in the control or suppression of commercially important diseases in various field crops horticultural crops and turf.

As the active ingredient in Evito 480 SC Fungicide, fluoxastrobin provides an effective tool for the management of a range of commercially important diseases including rusts, powdery mildew, blights, frogeye leaf spot, anthracnose and dollar spot. The product is applied as a preventative treatment on wheat, barley, corn, soybean, potato, tomato, pepper, strawberry and turf. As a new active ingredient in the class of strobilurin fungicides, Evito 480 SC Fungicide will provide increased competition in the Canadian agricultural fungicide market.

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 Evito 480 SC Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The label must include the following restriction for wheat forage: “If wheat forage will be harvested, make only one application.”

Because there is a concern with users coming into direct contact with Evito 480 SC Fungicide on the skin or through inhalation of spray mists, anyone mixing/loading and applying Evito 480 SC Fungicide must wear a long-sleeved shirt, long pants, shoes plus socks, and chemical resistant gloves. In addition, standard label statements to protect against drift during application are required.

Environment

To protect sensitive aquatic species from the use of fluoxastrobin, mitigation measures are recommended. These include adding precautionary statements to the label regarding environmental hazards and the directions for use, as well as no-spray buffer zones of up to 1 m for freshwater habitats and 10 m for marine habitats to mitigate potential exposures via spray drift.

Next Steps

Before making a final registration decision on fluoxastrobin, the PMRA will consider all 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 note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to 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 section 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 Ingredients and End-Use Product

Technical Product— Fluoxastrobin Technical Fungicide

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
Density	1.4216 g/mL at 25°C
Vapour pressure at 20°C	5.63 x 10^{-10} Pa
Ultraviolet (UV)-visible spectrum	λ_{max} = 250 nm
Solubility in water	pH / Solubility (mg/L) un-buffered 2.559 4 2.431 7 2.292 9 2.272

Property	Result
Solubility in organic solvents at 20°C	Solvent Solubility (g/L) n-heptane 0.04 1-octanol 1.09 2-propanol 6.7 xylene 38.1 polyethylene glycol 118.5 acetone >250 acetonitrile >250 dichloromethane >250 dimethyl sulfoxide >250 ethyl acetate >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— Evito 480 SC Fungicide

Property	Result
Colour	Off-white
Odour	Not available
Physical state	Liquid
Formulation type	Suspension
Guarantee	480 g/L
Container material and description	250 mL to 750 L HDPE container
Density at 20°C	1.10 g/cm^3
pH	6.8 (10% solution in distilled water)
Oxidizing or reducing action	Neither an oxidizing nor a reducing agent
Storage stability	Stable for one year in HDPE containers at ambient temperature
Corrosion characteristics	No corrosion to the HDPE container during one year storage
Explodability	Not expected to be explosive on the basis of the chemical nature of the formulation ingredients

1.3 Directions for Use

Fluoxastrobin, contained in Evito 480 SC Fungicide, is used to control stem rust and powdery mildew on wheat and barley, common rust and southern leaf blight on corn, frogeye leaf spot on soybean and anthracnose on strawberry. It is also used to suppress late blight on potato, tomato and pepper. The product is applied preventatively as a foliar treatment at rates ranging from 146 to 296 mL/ha on agricultural crops and 500 to 1000 mL/ha on turf. This results in a rate range for fluoxastrobin of 70 to 142 g/ha and 240 - 480 g/ha on agricultural crops and turf, respectively.

1.4 Mode of Action

Evito 480 SC Fungicide is a foliar applied, translaminar, systemic fungicide with preventative activity against certain diseases. The active ingredient, fluoxastrobin, is a strobilurin fungicide that inhibits fungal mitochondrial respiration which in turn interferes with spore germination, spore penetration, and mycelial growth.

2.0 Methods of Analysis

2.1 Methods for Analysis of Fluoxastrobin Technical Fungicide

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

2.2 Method for Formulation 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. Methods for residue analysis are summarized in Appendix I, Table 1.

2.3 Methods for Residue Analysis

The LC-MS/MS (liquid chromatography with tandem mass spectrometry) methods (Method#s 00604, 00649, 00668 and 00691) were developed and proposed for data gathering and enforcement purposes in plant and livestock commodities. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices. The proposed enforcement methods (Method#s 00604, 00649 and 00691) were successfully validated by an independent laboratory using respective samples. Adequate extraction efficiencies were demonstrated using radiolabelled plant and livestock samples in the metabolism studies.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for the technical grade active ingredient, fluoxastrobin, was conducted. 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.

Fluoxastrobin is a member of the strobilurin class of pesticides. This class of pesticides impairs energy function in the mitochondria. Fluoxastrobin (also known as HEC 5725) is proposed for registration as 98.8% E-isomer and 1.2% Z-isomer. Four-week studies in rats were performed to demonstrate chemical equivalence with two different isomer ratios. The test material referred to as HEC 5725 N contains 90% E-isomer and 10% Z-isomer, while a second test material referred to as HEC 5725 A contains 62.5% E-isomer and 35.2% Z-isomer. Based on the results of these studies, both isomer variants had similar toxicological profiles to the proposed version of fluoxastrobin and, as such, demonstrate a chemical equivalence.

In single-dose rat oral metabolism studies, radiolabelled fluoxastrobin was rapidly absorbed with peak blood concentrations (T_{max}) between 0.17 hours in low dose studies and up to 8 hours in high-dose studies while repeat dose testing resulted in a T_{max} of 0.95 hours. The half-life of elimination ($t_{1/2}$ e) was biphasic, indicating enterohepatic circulation. Elimination was primarily faecal via the bile. There were limited differences between the sexes with respect to absorption and elimination; however, differences between the low and high doses indicate that there is a saturation of absorption in the high-dose groups. There was no evidence of bioaccumulation and the highest level of radioactive residues were in the liver, kidneys and urinary bladder. Other organs with significant radioactive residues consisted of the mucosal wall of the stomach (with lower levels in the lumen of the stomach), blood, brown fat, perirenal fat, adrenal gland, skin, thyroid gland, pituitary gland and/or lung. By 168 hours, all radioactivity was below the limit of detection. Fluoxastrobin was extensively metabolized with no significant differences noted between the sexes or dose groups. The parent compound comprised 0.5-7.6% of the administered dose (AD) in the low dose groups and 43-54% of the AD in high dose groups. The major metabolic route was hydroxylation and methoxylation of the parent compound followed by further conjugation with glucuronic acid. The second major metabolic route was the cleavage of the chlorophenyl moiety from the parent compound resulting in des-chlorophenyl metabolites.

Following acute dosing, fluoxastrobin was found to be of low oral, dermal and inhalation toxicity in rats. It was minimally irritating to the eyes and non-irritating to the skin of rabbits. It was not a dermal sensitizer in guinea pigs.

The end-use product, Evito 480 SC Fungicide, was of low acute oral, dermal and inhalation toxicity in rats. It was non-irritating to the eyes and slightly irritating to the skin of rabbits. It was a potential skin sensitizer in guinea pigs.

After repeated oral dosing, the liver was a primary target in all species tested. In rodents, standard clinical chemistry enzymes were decreased, if affected, while proliferation-related enzymes were increased. In dogs, the standard clinical chemistry enzymes as well as the proliferation-related enzymes were increased. All three species exhibited increased liver weights and histopathological changes. In rats, triglycerides and bilirubin concentrations were decreased. In dogs, cholesterol was decreased; however, testosterone hydroxylases were increased in both sexes and greatly increased in females.

In addition to the liver, the kidney is a target of fluoxastrobin toxicity. These effects were primarily found in dogs and rats, while, in mice, changes were limited to hydropic degeneration in the kidneys of females in the 28-day study.

In the 90-day toxicity study in rats, serum calcium was increased at the high-dose level in both sexes. Urinary calcium oxalate levels were increased in males as were incidences of thickened walls of the urinary bladder, bladder stones, calculi formation, renal diffuse hyperplasia of the transitional epithelium, dilation of the pelvis and inflammation of the urinary bladder, with recovery noted in the majority of males. In the 24-month toxicity study in rats, urinary pH was increased while urinary volume, and potassium concentrations and excretion were decreased in both sexes. Calcium concentrations and excretion were decreased in females only. Kidney weights were increased at the highest dose tested in males and females. Males also exhibited kidney surface changes, cysts, renal tubular dilation, glomerular dilation and arteritis/periarteritis. When exposed to fluoxastrobin at the limit dose, females had decreased calcium in the femurs and bone ash.

In addition to the guideline toxicity studies in rats, there were non-guideline 60-day and metabolism studies to investigate urinary and nephritic effects. The 60-day toxicity study was performed with five dose levels per sex. An additional control and high-dose group were given 1% ammonium chloride (NH_4Cl) dissolved in the drinking water to determine the effects of acidifying the animals' urine on crystal formation. In addition to the aforementioned changes noted in the subchronic and chronic toxicity studies, males exhibited decreased serum S-bile acid, increased urinary oxalic acid excretion, increased bacterial count and increased uniformly small cytoplasmic vacuolation of the adrenal glands. Both sexes exhibited increased plasma calcium and unbound plasma calcium, an increased calcium to creatinine clearance and increased calcium oxalate crystal formation. Rats also exhibited an increased serum citric acid concentration. When given 1% NH_4Cl in their drinking water, a substance that in known to lower urinary pH, there was a decreased incidence of calcium oxalate crystal formation in males. Co-treatment with 1% NH_4Cl and fluoxastrobin maintained the urinary pH at a similar level as that of the main control animals and did not result in decreased serum and urinary calcium levels.

A non-guideline metabolism study in rats was performed to clarify the mechanism of hypercalciurea and calcium oxalate formation noted in the 90-day dietary toxicity study. Rats were treated with [^{45}Ca]chloride or [^{33}P]orthophosphate for 48 hours under continuous exposure to fluoxastrobin. In rats treated with [^{33}P]orthophosphate, decreased phosphorus absorption was accompanied by decreased urinary phosphorus excretion, resulting in decreased phosphorus uptake in the bone. In rats treated with [^{45}Ca]chloride, increased urinary calcium levels were attributed to the reduction of tubular calcium reabsorption and attributed to decreased phosphorus absorption.

In dogs, serum calcium was decreased in both sexes. In the 90-day study, kidney weights were increased along with an increase in degeneration of the proximal tubular epithelial cells of the kidneys in males. In a 12-month toxicity study, terminal kidney weights were increased in both sexes.

Overall, the major urinalysis changes observed in 60-day rat toxicity study explain the formation of calcium oxalate and corresponding urinary tract lesions observed in the previous subchronic rat dietary studies. The effects of fluoxastrobin on phosphorus and calcium levels observed in the non-guideline metabolism study were consistent with the 90-day dietary study in rats and the 60-day non-guideline dietary study in rats and indicated that altered phosphorus and calcium homeostasis were attributed to reduced phosphorus absorption.

In the combined chronic/carcinogenicity study in rats, there was a treatment-related increase in malignant uterine adenocarcinomas, increased vaginal bleeding, uterine nodules and focal uterine glandular hyperplasia in rats. However, the tumours occurred at the limit dose and in the presence of excessive toxicity including an 18% decrease in body weight and a 36% decrease in body weight gain. As a result, they were not considered relevant for the human risk assessment. The genotoxicity battery on the technical was determined to be negative with one equivocal in vitro study. Genotoxicity studies were performed on HEC 5725-E-des-chlorophenyl, the major metabolite in rats and also present in the soil, plants, and water. Two of the three studies were negative and one was considered equivocal. Overall the genotoxicity studies were considered negative.

In the reproductive toxicity study in rats, parental animals exhibited decreased body weight and body weight gain, increased food consumption (and, therefore, decreased food efficiency) and increased liver weights at the highest doses tested. At the same doses, offspring exhibited decreased body weight and body weight gain, a delay in preputial separation and incomplete ossification of the calvarium. This occurred in the presence of maternal toxicity and was not considered to represent sensitivity of the young. Special investigations were performed to determine whether the administration of fluoxastrobin affected the calcium and phosphorus content of the bones in utero and no effects were found. In the rat developmental toxicity study, there were liver changes in the dams and no treatment-related effects seen in the fetuses. In the rabbit developmental toxicity study, there were body weight and food consumption decreases in the dams and no treatment-related effects in the fetuses. In the rest of the database, changes to the reproductive system consisted of enlargement and discolouration of seminal vesicles in the 18-month mouse chronic toxicity study and the aforementioned hormonal changes in dogs.

There were no treatment-related effects in the 28-day dermal toxicity study in rats. There was no evidence of neurotoxicity in the acute or short-term neurotoxicity studies in the rat. Changes to the immune system were noted in a number of studies. In the 14-day mouse dietary toxicity study, leukocyte counts were decreased in males. In the 28-day dietary toxicity study in rats, the bone marrow cell counts were decreased in males, immunoglobulin A (IgA) levels were decreased in females at the second highest dose and increased lymph node cell counts were increased in both sexes at the highest dose tested. In the 90-day rat dietary toxicity study, immunoglobulin G (IgG) concentrations were decreased in males, along with spleen weights. A 5-week immunotoxicity study in mice was performed using a spleen immunoglobulin M (IgM) response to sheep red blood cells (sRBC); however, there was inadequate information in the report to interpret results of the plaque-forming cell (PFC) assay. With the exception of an increase in the number of mast cells in the mesenteric lymph nodes, there was no evidence of immunotoxicity in the 24-month chronic dietary toxicity study in the rat. In the 90-day toxicity

study in dogs, signs of immunotoxicity were limited to decreased spleen weights in males and decreased thymus weights in females.

Results of the toxicology studies conducted on laboratory animals with fluoxastrobin and its associated end-use product are summarized in Appendix I, Tables 2 and 3. The toxicology endpoints for use in the human health risk assessment are summarized in Appendix I, Table 4.

Incident Reports

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the PMRA website. Incidents from Canada and the United States were searched for fluoxastrobin, or any additional information submitted by the applicant during the review process was considered. As of December 19, 2011, there were no health-related incidence reports for this active in the PMRA Incident Reporting database.

3.1.1 PCPA Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the PCPA requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, extensive data were available for fluoxastrobin. The database contains the full complement of required studies including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, there was no indication of increased susceptibility of fetuses or offspring compared to parental animals in the reproductive and developmental toxicity studies. No developmental effects were observed in the rat and rabbit developmental toxicity studies. In the 2-generation rat reproductive toxicity study, preputial separation was delayed in the offspring at the highest dose tested. Other offspring effects noted at the highest dose tested included decreased body weight, thymus and spleen weights and incomplete ossification of the calvarium. However, these effects occurred in the presence of maternal toxicity (liver and body weight effects). Overall, there was a low concern for sensitivity of the young as endpoints in the young were well-characterized and not considered serious in nature. On the basis of this information, the PCPA factor was reduced to 1-fold.

3.2 Determination of Acute Reference Dose

As there were no effects in the toxicological database attributable to a single exposure of fluoxastrobin, an acute reference dose (ARfD) was not established.

3.3 Determination of Acceptable Daily Intake

To estimate dietary risk of repeat exposure, the 12-month dietary dog study with a no observed adverse effect level (NOAEL) of 1.5 mg/kg bw/day was selected for risk assessment. At the lowest observed adverse effect level (LOAEL) of 8.1/7.7 mg/kg bw/day in males/females, increased alkaline phosphatase (AP), liver weights and hepatocytomegaly were observed in males and females along with decreased body weights in females. This study provides the lowest NOAEL in the database. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the PCPA Hazard Characterization section, the PCPA factor was reduced to 1-fold. **The composite assessment factor (CAF) is 100-fold.**

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{1.5 \text{ mg/kg bw/day}}{100} = 0.015 \text{ mg/kg bw/day of fluoxastrobin}$$

The acceptable daily intake (ADI) provides a margin of greater than 49 000 to the dose at which preputial separation was delayed in the second generation male rat offspring and a margin of 1600 to testosterone hydroxylation in dogs.

Cancer Assessment

Since there was no evidence of oncogenicity at doses not exceeding the maximum tolerated dose, a cancer risk assessment was not conducted.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Short- and Intermediate-term Dermal

For short- and intermediate-term dermal risk assessment, the 21-day dermal toxicity study in rats was selected. This study was conducted by the relevant route of exposure and examined the critical endpoints of liver and kidney. There were no treatment-related effects at the NOAEL and highest dose tested of 1000 mg/kg bw/day.

The target margin of exposure (MOE) for these scenarios is 100, which accounts for interspecies extrapolation and intraspecies variability. The selection of this endpoint and target MOE was considered to be protective of all populations including nursing infants and the unborn children of exposed female workers.

Short- and Intermediate-term Inhalation

For short- and intermediate-term inhalation risk assessment, the NOAEL of 3 mg/kg bw/day from the 90-day dietary dog toxicity study was selected, since there were no repeat-dose inhalation studies submitted for this chemical. The NOAEL was based on decreased body weights, body weight gains and terminal body weights, decreased food consumption, changes in clinical chemistry parameters, increased liver enzyme activity levels, increased liver weights associated with hepatocytomegaly, decreased spleen weights (males only), decreased thymus weights (females only) and increased kidney weights associated with degeneration of the proximal tubular epithelium (males only) at the LOAEL of 24.8/24.2 mg/kg bw/day (males/females).

The target MOE for these scenarios is 100, which accounts for interspecies extrapolation and intraspecies variability. The selection of this endpoint and target MOE was considered to be protective of all populations including nursing infants and the unborn children of exposed female workers.

Non-Dietary Oral Ingestion (Children, Short-term)

For non-dietary oral ingestion risk assessment, the NOAEL of 3 mg/kg bw/day from the 90-day dietary dog toxicity study was selected. The NOAEL was based on decreased body weights, body weight gains and terminal body weights, decreased food consumption, changes in clinical chemistry parameters, increased liver enzyme activity levels, increased liver weights associated with hepatocytomegaly, decreased spleen weights (males only), decreased thymus weights (females only) and increased kidney weights associated with degeneration of the proximal tubular epithelium (males only) at the LOAEL of 24.8/24.2 mg/kg bw/day (males/females).

The target MOE for this scenario is 100, which accounts for interspecies extrapolation and intraspecies variability. As outlined in the PCPA Hazard Characterization section, the PCPA factor was reduced to 1-fold.

Occupational exposure to Evito 480 SC Fungicide is characterized as short- to intermediate-term and is predominantly by the dermal and inhalation routes.

3.4.1.1 Dermal Absorption

Dermal absorption data were not required as dermal risks were based on a dermal toxicity study.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to Evito 480 SC Fungicide during mixing/loading and application. Exposure to workers mixing/loading and applying Evito 480 SC Fungicide 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 chemical handlers applying Evito 480 SC Fungicide to wheat, corn, soybeans, potatoes, tomatoes, peppers, strawberries and turf using groundboom application equipment, as well as a turf gun sprayer and a backpack sprayer for turf. The exposure estimates are based on mixers/loaders/applicators wearing a single layer and gloves.

Since chemical-specific data for assessing human exposures during pesticide handling activities were not submitted, dermal and inhalation exposure estimates for mixers/loaders and applicators (M/L/A) are based on data from the Pesticide Handlers Exposure Database (PHED) and the Outdoor Residential Exposure Task Force (ORETF) of which the applicant is a member. PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. With a few exceptions, the PHED estimates meet criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides. All data were normalized for amount of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part. Inhalation exposures were based on light inhalation rates. ORETF data for turf gun applicators were used. The median measure of central tendency was used for dermal and inhalation unit exposures for liquid flowable formulations for workers wearing long pants, a long-sleeved shirt and gloves.

Table 3.4.1 Input Parameters for Mixers/Loaders and Applicators Risk Assessment

Scenario	Area Treated per Day (ha)	Unit Exposure (µg/kg a.i. handled)	
		Dermal	Inhalation
Groundboom Farmer	26	84.12	2.56
Groundboom Farmer – large field crops	107	84.12	2.56
Groundboom Custom – large field crops	360	84.12	2.56
Groundboom Turf- Sod farm	30	84.12	2.56
Turf gun sprayer	2	785	4
Backpack sprayer (turf)	0.4	5446	62.1

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 70 kg adult body weight.

A clothing scenario of long pants, long-sleeved shirts and gloves was assumed for handlers and workers applying Evito 480 SC to turf using a turf gun or backpack sprayer. Groundboom applicator risk was assessed for workers not wearing gloves. Exposure estimates were compared to the toxicological endpoints (NOAEL) to obtain the MOE. The target MOE for both routes of exposure is 100. Exposure and risk estimates for fluoxastrobin are presented in Table 2. Calculated risks for all scenarios are well above the target MOE and are not of concern.

Table 3.4.2 Exposure and Risk Estimates for Mixer/Loader/Applicators Handling Evito 480 SC Fungicide

Crop	Application Equipment	Maximum Rate (kg a.i./ha)	Dermal Exposure[1] (mg/kg bw/day)	Inhalation Exposure[1] (mg/kg bw/day)	Dermal MOE[2] Target=100	Inhalation MOE[3] Target=100
Cereals, Corn and Soybeans	groundboom farmer	0.14	0.018	0.00055	55550	5476
	groundboom custom	0.14	0.061	0.0018	16511	1628
Tomato and Pepper	groundboom farmer	0.13	0.0042	0.00013	240643	23722
Potato	groundboom farmer	0.133	0.017	0.00052	58474	5764
	groundboom custom	0.133	0.058	0.0018	17380	1713
Strawberry	groundboom	0.13	0.0032	0.00010	310502	30609
Turf – golf course, sod farm, residential turf	groundboom	0.480	0.017	0.00053	57788	5697
	Turf gun sprayer	0.480	0.011	0.00005	92887	54688
	Backpack sprayer	0.480	0.015	0.00017	66945	17613

[1] Exposure = (Unit exposure (µg/kg a.i. handled) × Application rate (kg a.i./ha) x Area treated per day (ha) /(70 kg bw × 1000 µg/mg)
[2] Based on NOAEL = 1000 mg /kg bw/day, target MOE = 100
[3] Based on NOAEL = 3 mg /kg bw/day, target MOE = 100

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for workers entering treated fields to perform routine re-entry activities to be exposed to residues of fluoxastrobin on foliage. Exposure is expected to be of short- to intermediate-term in duration and to occur primarily by the dermal route.

Since no chemical specific dislodgeable foliar residue (DFR) data were submitted, a default DFR value of 20% of the application rate with a 10% daily dissipation rate was used to estimate the amount of residues that may dislodge from treated foliage. For turf, a default turf transferable residue (TTR) value of 5% of the application rate with a 10% daily dissipation rate was used. A Tier 1 approach was used in that the highest transfer coefficient for each crop group was used to estimate exposure. Dermal exposure was calculated by coupling the DFR or TTR value on the day of application with the transfer coefficient and an 8-hour exposure duration. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight.

Calculated risks for fluoxastrobin are well above the target MOE for all crops and activities and are not of concern (Table 3.43).

Table 3.4.3 Postapplication Exposure and Risk Estimates for Evito 480 SC Fungicide

Crop	Re-entry Activity	Maximum Application Rate (kg a.i./ha)	Max Number of Application s/season	Transfer Coefficien t (cm^2/hr)	DFR or TR Value (µg/cm^2)	Dermal Exposure[1] (mg/kg bw/day)	Dermal MOE[2] Target= 100
Wheat and Barley	irrigation and scouting	0.14	2 on a 14-day interval	1500	0.3441	0.059	16952
Tomatoes and Peppers	hand harvesting, staking, tying, hand pruning, thinning, training	0.13	4 on a 7-day interval	1000	0.4832	0.055	18108
Corn (field, sweet and seed)	irrigation, scouting, hand weeding	0.14	4 on a 7-day interval	1000	0.5159	0.059	16961
	hand harvesting, and detasseling	0.14	4 on a 7-day interval	17000	0.5159	1.00	998
Soybeans	scouting, irrigation	0.14	4 on a 14 day interval	1500	0.3672	0.063	15886
Potato	scouting, irrigation	0.133	6 on a 7-day interval	1500	0.5038	0.086	11579
	hand harvest (sweet potatoes)			2500	0.5038	0.14	6947
Strawberry	hand harvesting, thinning, hand pruning, tying, training	0.13	4 on a 14-day interval	1500	0.3465	0.059	16835
Turf	transplanting and harvesting on sod-farms	0.480	4 on a 14-day interval	6800	0.3103	0.24	4147

[1] Exposure (µg/kg bw/day)= DFR ug/cm^2 (or TTR) x Transfer Coefficient cm^2/hr x Exposure Duration (8 hrs) /(70 kg bw × 1000 µg/mg)

[2] Based on NOAEL = 1000 mg /kg bw/day, target MOE = 100

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Postapplication Exposure and Risk

There is potential for acute and short- to intermediate-term exposure to adults and children through contact with transferable residues following commercial application of Evito 480 SC Fungicide to residential and recreational turf. As no acute risks were identified for fluoxastrobin, only short- to intermediate-term exposure and risk has been considered.

Based on the USEPA *Draft Standard Operating Procedures for Residential Exposure Assessments*, dermal exposure estimates were generated for adults and toddlers and non-dietary oral exposure estimates were generated for toddlers based on the following equations:

$$\textbf{Dermal Exposure (µg/kg bw/day)} = \frac{\textbf{TTR x TC x Duration}}{\textbf{bw}}$$

Where:

TTR:	Transferable turf residues are expressed as a percent of the applied rate. A peak value of 0.3103 µg/cm^2 was used in the assessment. A TTR value of 5% of the application rate (480 g a.i./ha), a maximum of 4 applications made 14 days apart, and a 10% default dissipation rate were assumed.
TC:	Transfer coefficients, expressed in cm^2/hr, are 7300 and 2600 cm^2/hr for adults and children, respectively, for short- to intermediate-term scenarios
Duration:	2 hours of continuous contact with treated turf
bw:	Body weight, is 70 kg for adults and 15 kg for toddlers

$$\textbf{Hand-to-mouth Exposure (µg/kg bw/day)} = \frac{\textbf{TTR x SA x Hand-to-mouth events x SEF x Duration}}{\textbf{bw}}$$

Where:

TTR:	Turf transferable residues (TTRs) are expressed as a percent of the applied rate. A TTR value of 5% of the application rate (480 g a.i./ha), a maximum of 4 applications made 14 days apart, and a 10% default dissipation rate were assumed (3.103 µg/cm^2).
SA:	Surface area of a child's hands, is 20 cm^2 which represents the area of 2 to 3 fingers
Hand-to-mouth events:	expressed in events/hr, 9.5 events/hour with 100% reloading of the hands between each event is assumed for short- to intermediate-term exposure
SEF:	Saliva extraction factor, is 50%
Duration:	2 hours of continuous contact with treated turf
bw:	body weight, is 15 kg for toddlers

Turf Mouthing/Ingestion Exposure = $\frac{\text{GR x Area of turf}}{\text{bw}}$
(µg/kg bw/day)

Where:

GR:	Grass residue expressed as a percent of the application rate. A value of 1.241 µg/cm^2 was used in the risk assessment (assuming a default value of 20% and a 10% dissipation rate per day).
Area of turf:	Expressed in cm^2/day. 25 cm^2 of turf mouthed/day is the amount that can be grasped in one handful
bw:	Body weight, is 15 kg for toddlers

Ingestion of Soil Exposure = $\frac{\text{APR x IR}_S\text{ x F x CF}}{\text{bw}}$
(µg/kg bw/day)

Where:

APR:	Application rate expressed in µg/cm^2, the maximum rate of 4.80 µg/cm^2 (480 g a.i./ha) is used.
IR_S:	Ingestion rate expressed in g/day. 0.1 g of soil is consumed in a single event
F:	Fraction of a.i. available in uppermost 1 cm of soil, expressed as fraction/cm (100% of the application rate/cm, which equals 4.80 μg/cm^3) (USEPA, 2001b), is used on the day of application.
CF:	Conversion factor to convert the volume units (cm^3) to weight units; 0.67 cm^3/g soil (USEPA, 1997).
bw:	Body weight, is 15 kg for toddlers

Incidental oral exposures (hand-to-mouth, turf mouthing and ingestion of soil) are combined, but apply only to toddlers on turf. Dermal and incidental oral exposure and risks are presented in Table 4. MOEs for all populations are well above the target MOE and are not of concern. No acute toxicological concerns were identified for fluoxastrobin. As such, only short- to intermediate-term MOEs are presented.

Table 3.4.4 Adult and Child Postapplication Exposure Estimates for Risk Exposure on Residential Lawns

Scenario	Dermal Exposure [1] (mg/kg/d)	Oral Exposure (mg/kg/d)			Dermal MOE [5]	Oral MOE[5]
		hand-to-mouth [2]	turf mouthing[3]	ingestion of soil [4]		
Adult (70 kg)						
Short- to Intermediate-term (1-30 days)	0.065	n/a	n/a	n/a	15451	n/a
Toddler (15 kg)						
Short- to Intermediate-term (1-30 days)	0.11	0.0039	0.0021	0.000021	9296	498

[1] Dermal exposure = TTR x TC x duration / bw (70 kg for adults, 15 kg for toddlers). TCs are 7300 and 2600 cm^2/hr for adults and toddlers, respectively for short- to intermediate-term scenarios. Exposure duration is 2 hrs. TTR value = 0.3103 μg/cm^2 based on a TTR value of 5% of the application rate, 4 applications made 14 days apart, and assuming a 10% daily dissipation rate.
[2]Exposure = TTR x SA x hand-to-mouth events x SEF x duration/15 kg bw. Based on 9.5 events/hr for intermediate- term scenarios, a surface area of 20 cm^2, saliva extraction factor (SEF) of 50%. TTR value = 0.3103 μg/cm^2 based on a TTR value of 5% of the application rate, 4 applications made 14 days apart, and assuming a 10% daily dissipation rate.
[3]Exposure = DFR x turf ingestion/15 kg bw. DFR = 20% of the application rate (1.241 μg/cm^2 assuming 4 applications made 14 days apart and a 10% daily dissipation rate. Ingestion = 25 cm^2 turf/day.
[4]Exposure = application rate x fraction of pesticide in soil x ingestion rate x soil density /15 kg bw. Based on 100% application rate available/cm (4.80 μg/cm^2); an ingestion of 0.1 g soil/day; and 0.67 cm^3/g soil weight to volume conversion factor.
[5]Based on a dermal NOAEL of 1000 mg/kg bw/day (target MOE is 100) and an oral NOAEL of 3 mg/kg bw/day for toddlers (target MOE is 100) for acute dermal and short- to intermediate-term scenarios.
n/a = not applicable

There is potential for short- to intermediate-term dermal exposure to adults and adolescents golfing on turf treated with Evito 480 SC Fungicide. Exposure estimates were generated based on the following equation:

$$\textbf{Dermal Exposure (μg/kg bw/day)} = \frac{\textbf{TTR x TC x Duration}}{\textbf{bw}}$$

Where:

TTR: Turf transferable residues are expressed as a percent of the applied rate. A TTR value of 5% of the application rate (480 g a.i./ha), a maximum of 4 applications made 14 days apart, and a 10% default dissipation rate were assumed.

TC:	Transfer coefficient, expressed in cm^2/hr, based on a generic agricultural transfer coefficient of 500 cm^2/hr for workers aerating, fertilizing, pruning, scouting and mowing treated turf was utilized. Exposure from these activities is considered to be similar to golfing. Transfer coefficients based on a body weight of 70 kg were scaled for the surface area of a 39 kg youth (correction factor = 12,700 cm^2/18,440 cm^2 = 68.9%) As such, the transfer coefficients are 500 and 344 cm^2/hr for adults and youth, respectively.
Duration:	4 hours/day of golfing activities
bw:	Body weight, is 70 kg for adults and 39 kg for youths

Exposure and risk estimates for adults and youths exposed to treated turf on golf courses are presented in Table 3.4.5. Calculated risks for all populations are well above the target MOE and are not of concern.

Table 3.4.5 Postapplication Exposure and MOEs for Golfers

Scenario	Dermal Exposure [1] µg/kg/d	Dermal MOE [2]
Adults (70 kg)		
Short to Intermediate-term	0.018	56397
Youths (39 kg)		
Short to Intermediate-term	0.022	45670

[1]Dermal exposure = TTR (0.3103 µg/cm^2) x TC x duration/bw (70 kg for adults, 39 kg for adolescents). The TTR value is based on a TTR value of 5% of the application rate, 4 applications made 14 days apart, and assuming a 10% daily dissipation rate. TC is 500 cm^2/hr based on generic transfer coefficients for turf. Transfer coefficients are scaled for the surface area of a 39 kg body weight (68.9% correction factor). Duration is 4 hrs.

[2] Based on a dermal NOAEL of 1000 mg/kg bw/day (target MOE is 100).

Since the use of Evito 480 SC Fungicide is proposed for use on strawberries, which may be harvested at pick-your-own operations, risk for individuals harvesting at these facilities was considered. However, as there are no acute dietary concerns for fluoxastrobin, a pick-your-own assessment was not required.

When residential exposure is expected for a product, aggregate risk from residential uses and dietary sources must be considered. However, since dermal and oral toxicological endpoints are based on different effects, the dermal and oral risks were not combined and an aggregate assessment was not conducted.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, 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

The residue definition for risk assessment and enforcement is fluoxastrobin (sum of E and Z isomers) in plant commodities, and fluoxastrobin (sum of E and Z isomers) including the metabolite HEC7154 in livestock commodities. The LC-MS/MS enforcement analytical methods# 00604 and 00649 are valid for the quantitation of fluoxastrobin (sum of E and Z isomers) residues in plant matrices. The LC-MS/MS enforcement analytical method# 00691 is valid for the quantitation of fluoxastrobin (sum of E and Z isomers) and HEC7154 residues in livestock matrices. The residues of fluoxastrobin (sum of E and Z isomers) are stable in plant commodities when stored frozen (< -18°C) for up to 30 months. Processing factors are determined to be 1.3x in wheat bran and 9.4x in dried tomato. Theoretical processing factors of 25x in corn oil and 12x in soybean oil are used in the absence of acceptable processing studies. The anticipated residues [fluoxastrobin (E and Z isomers) plus the metabolite HEC7154)] are <0.02 ppm in milk, <0.02 ppm in muscle, 0.026 ppm in liver, 0.068 ppm in kidney and 0.040 ppm in fat of ruminant, and <0.02 ppm in poultry tissues and eggs. Supervised residue trials conducted throughout the United States and Canada using the end-use product containing fluoxastrobin at the supported rates in/on celery, corn (field and sweet), wheat, barley, soybean, potato, tomato, pepper, and strawberry are sufficient to support the proposed maximum residue limits.

3.5.2 Dietary Risk Assessment

Chronic dietary risk assessments were 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.

3.5.2.1 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 15.1% 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 21.7% (0.003254 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children of 1-2 years old at 45.1% (0.006772 mg/kg bw/day) of the ADI.

3.5.2.2 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.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for fluoxastrobin consists of exposure from food and drinking water sources only. Although there is a residential use on turf, the dermal and oral toxicological endpoints are not to be combined, since they were based on different effects. Furthermore, there was no acute endpoint identified for the general population, including infants and children, thus a pick-your-own assessment for strawberries was not required.

3.5.4 Exposure from Drinking Water

Concentrations in Drinking Water

Estimated environmental concentrations (EECs) of fluoxastrobin in potential drinking water sources (groundwater and surface water) were estimated using computer simulation models. An overview of how the EECs are estimated is provided in the PMRA's Science Policy Notice SPN2004-01, *Estimating the Water Component of a Dietary Exposure Assessment*. EECs of fluoxastrobin in groundwater were calculated using the LEACHM model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using LEACHM are based on the flux, or movement, of pesticide into shallow groundwater with time. EECs of fluoxastrobin in surface water were calculated using the PRZM/EXAMS models, 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 two types of vulnerable drinking water sources, a small reservoir and a prairie dugout.

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 EECs are expected to allow for future use expansion into other crops at this application rate. Table 3.4-1 lists the application information and main environmental fate characteristics used in the simulations. Twelve (eight for surface water and four for groundwater) initial application dates between May 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 3.4-2 below.

Table 3.5.4.1 Major groundwater and surface water model inputs for Level 1 assessment of fluoxastrobin

Type of Input	Parameter	Value
Application Information	Crop(s) to be treated	soybean, wheat, barley, corn, potato, tomato, pepper, strawberry, and turf
	Maximum allowable application rate per year (g a.i./ha)	1920 (turf); 798 (potato)
	Maximum rate each application (g a.i./ha)	480 (turf); 133 (potato)
	Maximum number of applications per year	4 (turf); 6 (potato)
	Minimum interval between applications (days)	14 (turf); 7 (potato)
	Method of application	Ground
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	Stable
	Photolysis half-life in water (days)	27.7
	Adsorption K_{OC} (mL/g)	657.8 (20^{th} percentile of four K_{OC} values for fluoxastrobin)
	Aerobic soil biotransformation half-life (days)	226 (80^{th} percentile of four half-life values)
	Aerobic aquatic biotransformation half-life (days)	382 (longest of two half-lives)
	Anaerobic aquatic biotransformation half-life (days)	715 (only value available)

Table 3.5.4.2 Level 1 estimated environmental concentrations of fluoxastrobin in potential drinking water

Compound	Groundwater EEC (g a.i./L)		Surface Water EEC (g a.i./L)			
			Reservoir		Dugout	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[3]	Yearly[4]
Fluoxastrobin	47	47	60	17	186	164

Notes:
1 90^{th} percentile of daily average concentrations
2 90^{th} percentile of yearly average concentrations
3 90^{th} percentile of yearly peak concentrations
4 90^{th} percentile of yearly average concentrations

Details of water modelling inputs and calculations are available upon request.

3.5.5 Maximum Residue Limits

Table 3.5.5.1 Proposed Maximum Residue Limit

Commodity	Recommended MRL (ppm)
Dried tomatoes	4.5
Crop Subgroup 4B (Leaf Petioles)	4.0
Crop Subgroup 13-07G (Low Growing Berry)	1.9
Tomato paste	1.5

Crop Group 8-09 (Fruiting Vegetables)	1.0
Corn oil	0.50
Soybean oil	0.40
Meat by-products of cattle, goat, horse, and sheep	0.20
Milk fat	0.15
Wheat bran	0.15
Crop Group 15 (Cereal Grains), except field corn, sweet corn, and popcorn	0.10
Fat of cattle, goat, horse, and sheep	0.10
Meat of cattle, goat, horse, and sheep	0.05
Dry soybeans	0.05
Eggs	0.02
Field corn	0.02
Popcorn grain	0.02
Fat, meat, and meat by-products of hogs and poultry	0.02
Milk	0.02
Crop Subgroup 1C (Tuberous and Corm Vegetables)	0.01
Sweet corn kernels plus cob with husks removed	0.01

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

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and the chronic dietary risk estimates are summarized in Appendix I, Tables 1, 5, and 6.

4.0 Impact on the Environment

Technical fluoxastrobin contains two isomeric forms (E/Z-isomers). The ISO name refers to the E isomer only. The test active substance used in studies generally contained 2.0-3.3 % Z isomer as an impurity. Conversion of the E- into the Z- isomer was observed in laboratory and field dissipation studies. This risk assessment was based on combined E- and Z- data, with the assumption that the toxicity of Z-isomer is equal or less than the E-isomer. Dissipation half-lives were also calculated with the combined E and Z- isomers.

Fluoxastrobin can be applied by field sprayer and there is a potential that non-target terrestrial and aquatic habitats may be exposed to the chemical as a result of spray drift or runoff. Fluoxastrobin has a low solubility in water and, based on its physical-chemical properties, it is not expected to volatilize. Based on results of a bioaccumulation study with bluegill sunfish, it was determined that fluoxastrobin in unlikely to bioaccumulate (Appendix I, 7).

In laboratory studies, fluoxastrobin has three major transformation products: fluoxastrobin-deschlorophenyl, formed in the aerobic soil and water/sediment studies, fluoxastrobin-carboxylic acid, formed in the aerobic and anaerobic water/sediments system studies, and fluoxastrobin-oxazepine, formed in the aqueous photolysis study. While these three transformation products were monitored in field studies, only fluoxastrobin-deschlorophenyl was reported as a major

transformation product; fluoxastrobin-carboxylic acid was measured in the field at low concentrations, and fluoxastrobin-oxazepine was not observed above the level of detection. A summary of the major transformation products, their maximum formation rate (as a percentage of applied radiation in the study) and time of maximum occurrence in each of the laboratory studies is presented in Appendix I, Table 8.

Soil adsorption studies conducted with fluoxastrobin and its two major transformation products fluoxastrobin-deschlorophenyl and fluoxastrobin-carboxylic acid, suggest that parent fluoxastrobin has a tendency to bind to soil and the transformation products may have a potential to leach in soil. In field dissipation studies, fluoxastrobin was detected in the top soil horizons only; which supports the findings of the laboratory studies indicating medium to low mobility. Fluoxastrobin-deschlorophenyl, on the other hand was detected in deeper soil layers. It is expected that fluoxastrobin's high binding affinity for soil will limit its movement into anaerobic soil.

Field and laboratory studies suggest that fluoxastrobin can persist in the terrestrial environment. While a large portion of fluoxastrobin residues bind to soil, fluoxastrobin can also biotransform to fluoxastrobin-deschlorophenyl under aerobic conditions. Based on available data, fluoxastrobin's major transformation products, fluoxastrobin-deschlorophenyl and fluoxastrobin carboxylic acid are not expected reach concentrations of concern to the environment.

Once in the water, fluoxastrobin is not expected to hydrolyse but can phototransform to fluoxastrobin-oxazepine in clear shallow water. In a water/sediment system, fluoxastrobin will partition to sediments due to its hydrophobic nature and high soil adsorption capacity.

Fluoxastrobin is persistent in sediments, but, under anaerobic conditions, it can undergo microbial degradation to fluoxastrobin-carboxylic acid. Binding to sediments constitutes a major route of dissipation. The environmental fate and behaviour of fluoxastrobin are summarised in Appendix I, Table 9.

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 concentrations 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 (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.

Exposure and toxicity information used for risk assessment is found in Appendix I, Tables 10-17. Tables 10, 11 and 12, respectively present screening level fluoxastrobin EECs in soil and plant surfaces, on vegetation and insects consumed by birds and mammals, and in water. Refined EECs for fluoxastrobin spray drift input to water are in Appendix I, Table 13, and for fluoxastrobin runoff input to water are in Appendix I, Tables 14 and 15. The toxicity endpoints for terrestrial and aquatic organisms are presented in Appendix I, Tables 16 and 17.

4.2.1 Risks to Terrestrial Organisms

Earthworms: Exposure of earthworms to fluoxastrobin could result from ingestion of treated soil. Earthworms are not expected to be at risk from the application of Evito 480 SC Fungicide at the proposed Canadian use rate. The acute and chronic risk to earthworms from either fluoxastrobin or the formulated Evito 480 SC Fungicide, at the proposed maximum application rate was less than the LOC (Appendix I, Table 18).

Pollinators: Acute oral and contact exposure to fluoxastrobin did not result in significant mortality or sublethal effects in honey bees. The resulting risk quotients for both acute contact and oral exposure routes were all below the LOC, indicating fluoxastrobin is not expected to pose a risk to pollinators (Appendix I, Table 18).

Predatory and Parasitic arthropods: The toxicity of fluoxastrobin was determined in laboratory studies with the preferred indicator species, the predatory mite *Typhlodromus pyri* and the aphid parasitoid, *Aphidius rhopalosiphi*, and also with the ladybird beetle, *Coccinella septempunctata* and the rove beetle *Aleochara bilineata*. The screening level risk quotients for the two indicator species exceeded the LOC for in-field exposure, but not for off-field exposure. Fluoxastrobin also reduced the survival of ladybird beetles exposed to fluoxastrobin spray deposits on glass plates and affected reproduction of rove beetles exposed to exposed to treated quartz sand. The in-field and off-field LOCs, based on mortality of ladybird beetles exposed to

fluoxastrobin on glass plates were exceeded (Appendix I, Tables 16 and 18). As a potential risk to certain predatory and parasitic arthropods was identified, a label statement will be required.

Birds: Fluoxastrobin has a low toxicity to birds. In acute oral and dietary studies conducted with the bobwhite quail and the mallard, fluoxastrobin had no treatment-related effects on mortality or clinical signs of toxicity and no treatment-related abnormalities were observed upon necropsy. Treatment related reductions in body weight change was observed at the higher concentrations in the dietary and reproduction studies with mallard duck, and egg production was also affected at the higher concentrations in a reproduction study with the mallard. In a reproduction study with the bobwhite quail, however, the highest concentration tested did not elicit an adverse effect on any parental or reproductive parameter (Appendix I, Table 16). Screening level risk quotients based on acute and chronic exposures of birds to fluoxastrobin were below the level of concern (Appendix I, Table 19).

Mammals: Environmentally relevant endpoints from acute and reproductive toxicity studies with the rat were used to determine risk to small terrestrial mammals. Fluoxastrobin is practically nontoxic to rat on acute basis and the reproductive NOAEL was 741.6 mg/kg bw/day. No risks were identified in the screening level risk assessment based on three size classes of small mammals using conservative assumptions for intakes of food sources (Appendix I, Table 19).

Terrestrial Plants: The toxicity of fluoxastrobin to non-target plants was determined through vegetative vigour and seedling emergence assays using standard crop species. No significant adverse effects were observed in any plant species in either the vegetative vigour or seedling emergence assays with formulated fluoxastrobin (SC 480, Appendix I, Table 16). The EC_{25} was not determined and the screening level risk quotient, based on the highest tested concentration was < 1.26 for seedling emergence and vegetative vigour (Appendix I, Table 18). As no adverse effects were noted in the study, and because the risk quotient is close to the level of concern, fluoxastrobin is not expected to pose a risk to non-target terrestrial plants at the proposed Canadian use rates.

4.2.2 Risks to Aquatic Organisms

Aquatic organisms can be exposed to fluoxastrobin as a result of spray drift and over-land run-off. To assess the potential for adverse effects, screening level EECs in the aquatic environment based on a direct application to water following application to turf were used as the exposure estimates. A risk assessment of fluoxastrobin and the transformation products fluoxastrobin-deschlorophenyl and fluoxastrobin-carboxylic acid was undertaken for freshwater and marine aquatic organisms based on available toxicity data for each of the compounds to invertebrates (acute and chronic), fish (acute and chronic), amphibians (using fish as surrogate data), and freshwater vascular plant and algae.

A summary of aquatic toxicity data for fluoxastrobin and the two transformation products fluoxastrobin deschlorophenyl and fluoxastrobin-carboxylic and a 65:35 mixture of the E- and Z-isomers of fluoxastrobin are presented in Appendix I, Table 17. For acute toxicity studies

uncertainty factors of 1/2 and 1/10 $EC(LC)_{50}$ are used in modifying the toxicity values for aquatic plants and invertebrates and fish species, respectively when calculating RQs. No uncertainty factors are applied to chronic no observed effect concentration (NOEC) endpoints. For groups where the LOC is exceeded (i.e., RQ ≥ 1), a refined assessment is conducted to determine potential risks resulting from spray drift and runoff separately.

Freshwater invertebrates: Results of acute toxicity tests with freshwater invertebrates are tabulated in Appendix I, Table 17. Based on the available data, the amphipod, *G. pulex*, appears to be most sensitive tested species.

Studies with the 65:35 mixture of the E- and Z- isomers of fluoxastrobin did result in effects on aquatic invertebrates (*D. magna)*, but no effects were for the transformation products, Fluoxastrobin-deschlorophenyl and fluoxastrobin-carboxylic acid, with acute exposures. No treatment-related parental mortality was observed during a 21-day life-cycle study with *D. magna.* The numbers of offspring per adult were decreased at the highest concentration tested.

Two 28-day subchronic studies were also submitted for fluoxastrobin and the transformation product fluoxastrobin-carboxylic acid, using the midge, *Chironomus riparius.* Fluoxastrobin affected the time and rate of development, but in the fluoxastrobin-carboxylic acid study, no delay in emergence was observed at any test concentration.

The acute and chronic screening assessment risk quotients exceeded the level of concern for freshwater aquatic invertebrates (Appendix I, Table 20). In the refined assessment, however, risk quotients were below the LOC for the spray drift and runoff exposure scenarios, indicating that fluoxastrobin is unlikely to be a risk to freshwater invertebrates.

Freshwater fish and amphibians: The toxicity of fluoxastrobin and the two major transformation products fluoxastrobin-deschlorophenyl and fluoxastrobin-carboxylic acid to fish was assessed for acute exposure considering toxicity studies from three species (rainbow trout, common carp and bluegill sunfish) and one species for sub-chronic exposure (rainbow trout).

In acute toxicity testing with rainbow trout *(Oncorhynchus mykiss)*, sublethal effects included loss of equilibrium, fish at the bottom of the test chamber, and quiescence. Similar sublethal effects were also noted in bluegill sunfish *(Lepomis macrochirus)*, and in common carp *(Cyprinus carpio)* exposed to the highest fluoxastrobin concentrations.

In a life-cycle study conducted with the rainbow trout, no treatment-related effects on hatchability, survival, and/or terminal growth parameters were observed. A reduction in time to swim up and an increase incidence in oversized yolk sacs were statistically different than control, but these endpoints were transient and, in the case of time to swim up, not dose dependent.

No mortality or sublethal effects on rainbow trout were observed at the highest tested concentrations in acute toxicity studies conducted with the transformation products fluoxastrobin-carboxylic acid and fluoxastrobin-deschlorophenyl.

The screening assessment risk quotients for freshwater fish exceeded the LOC (Appendix I, Table 20). In the refined risk assessment; however, RQs were below the LOC for the spray drift and runoff exposure scenarios.

In absence of toxicity data on an amphibian, a screening level risk assessment was conducted using fish toxicity endpoints as surrogates for aquatic life-stages of amphibians and EECs calculated for 15 cm deep water. Acute and chronic risks from fluoxastrobin were identified at the screening level (Appendix I, Table 20) and under refined estimates for exposure via spray drift (RQs up to 1.7 and 2.3 for runoff) (Appendix I, Table 21). Because a potential risk to amphibians was identified, label statements and no-spray buffer zones will be required.

Freshwater algae and plants: The acute toxicity of fluoxastrobin, and its transformation products fluoxastrobin-deschlorophenyl, and fluoxastrobin-carboxylic acid was tested on freshwater vascular plants and algae (Appendix I, Table 17). A reduction in frond number was observed in duckweed (*Lemna gibba*) exposed to fluoxastrobin, and a treatment related reduction in cell density was observed in freshwater green algae (*Selenastrum capricornutum*) exposed to fluoxastrobin and its transformation products fluoxastrobin-deschlorophenyl and fluoxastrobin-carboxylic acid. While cell density was the most sensitive endpoint for the parent and its transformation products, an EC_{50} could not be determined for fluoxastrobin-deschlorophenyl since only 12% reduction was observed at the highest tested concentration. The screening level risk quotient exceeded the LOC only for green algae exposed to fluoxastrobin. Results of the refined risk assessment, however, showed that freshwater plants and algae are not at risk from runoff or drift inputs (Appendix I, Table 21).

Marine species: Acute toxicity studies with fluoxastrobin were conducted with a variety of marine organisms. Marine invertebrates were identified as the most sensitive species (Appendix I, Table 17).

The marine invertebrate screening level and refined runoff exposure risk quotients exceeded the LOC (Appendix I, Tables 20 and 21). The screening and refined (runoff and spray drift) LOCs, based on acute exposure were also exceeded for the marine diatom, but the screening LOC was not exceeded for the mollusk acute endpoint.

In an acute toxicity test with the marine sheepshead minnow, no mortality or sub-lethal effects were observed in any test or control group following 96 hours of exposure. Because the highest tested concentration was below the screening level EEC, the PMRA used the refined risk quotients. These are below the level of concern for EECs calculated for spray drift and runoff (Appendix I, Tables 20 and 21).

Fluoxastrobin affected survival and caused sublethal effects in mysid shrimp (*A. bahia*) in a 28 day life cycle test. The LOC was exceeded for EECs calculated for spray drift and runoff for marine invertebrates (Appendix I, Tables 20 and 21). However, the scenario for determining EEC values, a closed shallow pond, is considered a very conservative representation for an open and variable marine or estuarine environment. Because a potential risk to marine invertebrates was identified, label statements and no-spray buffer zones will be required.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

Demonstrations of Evito 480 SC Fungicide efficacy against labelled pests were provided in a total of 13 trials.

5.1.1.1 Wheat and Barley

Stem rust

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against stem rust on wheat and barley. Under moderate to high disease pressure, Evito 480 SC Fungicide provided control of the disease by reducing severity by up to 100%. The submitted trial was conducted on wheat; however, because of the similarity in biology and disease development between the two crops, the evidence obtained from wheat can be extrapolated to support the disease claim on barley.

Powdery mildew

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against powdery mildew on wheat and barley. Under high disease pressure, Evito 480 SC Fungicide provided control of the disease, reaching up to 93% of reduction in severity. The submitted trial was conducted on wheat; however, because of the similarity in biology and disease development between the two crops, the evidence obtained from wheat can be extrapolated to support the disease claim on barley.

5.1.1.2 Corn

Common rust

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against common rust on corn. Under moderate to high disease pressure, Evito 480 SC Fungicide provided control of the disease, reaching up to 100% of reduction in severity. This level of control was comparable to those obtained from commercial standards.

Southern corn leaf blight

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against southern leaf blight on corn. Under moderate to high disease pressure, Evito 480 SC Fungicide provided up to 87% disease reduction 27 days after a single application. A second application of Evito 480 SC Fungicide is expected to prolong the protective effect of the product.

5.1.1.3 Soybean

Frogeye leaf spot

Three field trials were presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against frogeye leaf spot on soybean. Under disease pressures, which ranged from moderate to high across the submitted trials, Evito 480 SC Fungicide provided satisfactory reductions in disease severity. Reductions ranged from 80 to 100%.

5.1.1.4 Potato

Late blight

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against late blight on potato. Disease pressure in this trial was moderate. Evito 480 SC Fungicide treatments resulted in disease reductions of up to 87%. Additional support for this claim is extrapolated from another submitted trial conducted on the same disease but on tomatoes. In this trial, late blight reductions reached up to 100% under high disease pressure.

5.1.1.5 Tomato and Pepper

Late blight

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against late blight on tomato and pepper. Under high disease pressure, Evito 480 SC Fungicide provided high levels of disease reduction on tomato plants. Results obtained from a trial conducted on late blight in potatoes was also considered as supplemental support for this claim as Evito 480 SC Fungicide also showed good levels of efficacy against the same pathogen in this crop.

5.1.1.6 Strawberry

Anthracnose

One field trial was presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against anthracnose on strawberry. Under moderate disease pressure, Evito 480 SC Fungicide provided control of the disease, attaining up to 81% reductions in disease severity.

5.1.1.7 Turf

Dollar spot

Three field trials were presented to support the value assessment of the Evito 480 SC Fungicide efficacy claim against dollar spot on turf. Moderate to high disease pressure was present throughout the three trials. Under these conditions, Evito 480 SC Fungicide applied at 500-1000 mL/ha provided control levels attaining up to 95% and generally provided adequate protection

across the three trials. A trend towards higher levels of control was observed in the treatment with the high rate of Evito 480 SC Fungicide.

5.2 Phytotoxicity

No evidence of phytotoxicity was observed in any of the efficacy trials where adverse effects were assessed.

5.3 Economics

No market analysis was done for this application.

5.4 Sustainability

5.4.1 Survey of Alternatives

The chemical and other non-conventional/biological fungicidal active ingredients listed in Appendix I, Table 23 are found in products that are registered for control or suppression of diseases indicated on the Evito 480 SC Fungicide label. These registered alternatives are labelled for use on either an entire crop group or limited to certain crops within a listed crop group.

5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

In addition to the use of registered fungicides, pressure from diseases listed on the Evito 480 SC Fungicide label can be reduced through cultural practices such as planting tolerant or resistant cultivars, crop rotation, and ensuring that appropriate phytosanitary measures are followed. Evito 480 SC Fungicide would provide growers with an additional tool for management of diseases in the labelled crops and is not expected to interfere with preventative measures when used as recommended.

5.5.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Evito 480 SC Fungicide contains fluoxastrobin as its active ingredient. Fluoxastrobin is classified as a Group 11 Fungicide (Quinone ‘outer’ inhibitor). FRAC regards this group as posing a high risk for disease resistance development. Resistance to Group 11 fungicides has been documented for numerous fungal plant pathogens. FRAC reports resistance in various European countries to this group of fungicides by the pathogens that cause powdery mildew in wheat and barley. With the exception of corn, all of the crops on the Evito 480 SC Fungicide label are susceptible to at least one fungal pathogen in which FRAC reports resistance to Group 11 fungicides; however, none of the diseases that are caused by these pathogens currently appear on the Evito 480 SC Fungicide label. In order to reduce the risk of disease resistance development, specific use restrictions and recommendations for Evito 480 SC Fungicide and other Group 11 Fungicides appear on the label.

5.5.4 Contribution to Risk Reduction and Sustainability

Evito 480 SC Fungicide, with its active ingredient fluoxastrobin, provides an effective disease management tool for economically important crops in Canadian agriculture and horticulture. Its judicious use is compatible with current IPM recommendations.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e., persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, fluoxastrobin and its major transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Fluoxastrobin does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix I, Table 22 for comparison with Track 1 criteria.
- Fluoxastrobin does not form any transformation products that meet all Track 1 criteria. Two environmentally relevant fluoxastrobin major transformation products were identified. Fluoxastrobin-carboxylic acid has a log K_{ow} lower than the parent (1.83 to -0.46) and fluoxastrobin-deschlorophenyl is more soluble in water than fluoxastrobin, therefore its log K_{ow} value is expected to be lower than the parent. As such, the transformation products do not meet the Track 1 criteria.

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*[6]. The list

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

6 *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.*

is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8], 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:

The end-use product, Evito 480 SC Fungicide, contains trace amounts of chlorinated dibenzodioxins (maximum 8.49 x 10^{-11} %) and dibenzofurans (maximum 3.40 x 10^{-10} %). Based on the formulating process used, other impurities and formulants of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances and allergens known to cause anaphylactic-type reactions, are not expected to be present in the product or carried through from Fluoxastrobin Technical Fungicide. The PMRA is managing the presence of these contaminants in accordance with the Agency's strategy to prevent or minimize releases, with the ultimate goal of virtual elimination as described in DIR99-03.

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02[9].

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for fluoxastrobin is adequate to define the majority of toxic effects that may result from exposure. There was no evidence of carcinogenicity considered relevant to human risk assessment. There was no evidence of increased susceptibility of the young in reproduction or developmental toxicity studies. Fluoxastrobin is not neurotoxic. In short-term and chronic studies on laboratory animals, the primary targets were the liver, kidneys, and urinary bladder. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

The nature of the residue in plants and animals is adequately understood. The residue definition for enforcement and risk purposes is fluoxastrobin (sum of E and Z isomers) in plants, and fluoxastrobin (sum of E and Z isomers) including the metabolite HEC7154 in livestock commodities. The proposed use of fluoxastrobin on corn (field and sweet), wheat, barley, soybean, potato, tomato, pepper, and strawberry does not constitute an unacceptable chronic dietary risk (food and drinking water) to any segment of the population, including infants,

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

8 DIR2006-02, PMRA Formulants Policy.

9 DIR2006-02, PMRA Formulants Policy.

children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified for:

Commodity	Recommended MRL (ppm)
Dried tomatoes	4.5
Crop Subgroup 4B (Leaf Petioles)*	4.0
Crop Subgroup 13-07G (Low Growing Berry)	1.9
Tomato paste	1.5
Crop Group 8-09 (Fruiting Vegetables)	1.0
Corn oil	0.50
Soybean oil	0.40
Meat by-products of cattle, goat, horse, and sheep	0.20
Milk fat	0.15
Wheat bran	0.15
Crop Group 15 (Cereal Grains), except field corn, sweet corn, and popcorn	0.10
Fat of cattle, goat, horse, and sheep	0.10
Meat of cattle, goat, horse, and sheep	0.05
Dry soybeans	0.05
Eggs	0.02
Field corn	0.02
Popcorn grain	0.02
Fat, meat, and meat by-products of hogs and poultry	0.02
Milk	0.02
Crop Subgroup 1C (Tuberous and Corm Vegetables)	0.01
Sweet corn kernels plus cob with husks removed	0.01

Mixers, loaders and applicators handling Evito 480 SC Fungicide and workers re-entering treated areas are not expected to be exposed to levels of Evito 480 SC Fungicide that will result in an unacceptable risk when the Evito 480 SC Fungicide is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

Residential exposure to individuals contacting treated turf or pick-your-own establishments is not expected to result in unacceptable risk when Evito 480 SC Fungicide is used according to label directions.

*Celery is supported only as an import MRL at this time.

7.2 Environmental Risk

Fluoxastrobin is persistent in the terrestrial and aquatic environments and is not expected to volatilize to the atmosphere. Fluoxastrobin presents a negligible risk to earthworm, honeybee and terrestrial plants and vertebrates at the proposed use rates, but may pose a risk to predatory and parasitic arthropods. Fluoxastrobin poses a potential risk to freshwater invertebrates, amphibians and fish, and to marine invertebrates and algae. Label statements are proposed to identify to users the potential risks to aquatic organisms and beneficial terrestrial arthropods. In

order to minimize the potential for spray drift exposure, no-spray buffer zones between the treated area and downwind aquatic areas will be required and will be specified on the product label.

No environmental risk was identified from exposure to fluoxastrobin's major transformation products.

No environmental risk was identified from exposure to fluoxastrobin's major transformation products.

7.3 Value

The value data submitted in support of the various Evito 480 SC Fungicide claims demonstrated that the product could be used as an effective tool to control or suppress various economically important diseases on wheat, barley, corn, soybean, potato, tomato, pepper, strawberry, and turf grass.

7.4 Unsupported Uses

Although value was demonstrated for at least one or two disease claims on each of the crops on the Evito 480 SC Fungicide label, certain disease claims could not be supported at the time of this assessment because the information available was inadequate to substantiate efficacy against causal pathogens.

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 Evito 480 SC Fungicide, containing the technical grade active fluoxastrobin, to control or supress various economically important diseases on wheat, barley, corn, soybean, potato, tomato, pepper, strawberry and turf grass.

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

µg	micrograms
abs	absolute
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
AGF	aspirated grain fractions
ALD	aldrin-epoxidase
AP	alkaline phophatase
APR	application rate
ALT	alanine amino-transferase
AR	applied radioactivity
ARfD	acute reference dose
ASAE	American Society of Agricultural Engineers
AST	aspartate amino-transferase
AUC	area under the curve
BAF	Bioaccumulation Factor
BBCH	Biologishe Bundesanstalt, Bundessortenamt and Chemical industry
BCF	Bioconcentration Factor
bw	body weight
bwg	bodyweight gain
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CF	Conversion factor
cm	centimetres
CNB	could not be determined
d	day(s)
DALA	days after last application
DAT	days after treatment
DEEM-FCID	Dietary Exposure Evaluation Model
DFOP	double first-order in parallel
DFR	dislodgeable foliar residue
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
dw	dry weight
EC_{15}	effective concentration on 15% of the population
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
ECOD	7-ethoxycoumarin-deethylase
EDE	estimated daily exposure
EEC	estimated environmental concentration
EH	epoxide hydrolase
EROD	7-ethoxyresorufin-deethylase
F	Fraction
F_1	first generation
FC	food consumption
FDA	Food and Drug Act
FE	food efficiency

FRAC	Fungicide Resistance Action Committee
fw	fresh weight
g	gram
GD	gestation day
GIT	gastrointestinal tract
GLU-T	UDP-glucuronyl-transferase
GR	grass residue
GST	glutathione S-transferase
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
HDPE	high density polyethylene
HPLC	high performance liquid chromatography
hr	hour(s)
IgA	immunoglobulin A
IgG	immunoglobulin G
IgM	immunoglobulin M
ILV	independent laboratory validation
IORE	indeterminante order rate equation
IPM	Integrated Pest Management
IR_S	ingestion rate
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre(s)
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
MBDB	more balanced dietary burden
m	metre(s)
MAS	maximum average score
mg	milligram
mL	millilitre
M/L/A	mixers/loaders and applicators
MOE	margin of exposure
mPa	megapascals
MRL	maximum residue limit
MRM	multiresidue method
MS	mass spectrometry
MTD	Maximum tolerated dose
n/a	not applicable
ND	not detected

NH_4Cl	ammonium chloride
NIS	non-ionic surfactant
nm	nanometre
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NR	not relevant
NZW	New Zealand white
ORETF	Outdoor Residential Exposure Task Force
Pa	pascal
PBI	plantback interval
PCNA	proliferating cell nuclear antigen
PCPA	*Pest Control Products Act*
PFC	plaque-forming cell
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RAC	raw agricultural commodity
rel	relative
RTI	retreatment interval
SA	Surface area
SC	soluble concentrate
SEF	Saliva extraction factor
SFO	single first-order
SPE	solid phase extraction
sRBC	sheep red blood cells
$t_{1/2}$	half-life
$t_{1/2}e$	elimination half-life
TC	Transfer Coefficient
T_{max}	time to peak blood concentration
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
TTR	turf transferable residue
US	United States
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
WP	wettable powder
wt/wts	weight/weights

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Plant	00604	Fluoxastrobin (E and Z isomers)	LC-MS/MS	0.01 ppm (sum of E and Z isomers) for potato tuber, 0.02 ppm for cereal grains and vegetables (tomato, cucumber, onion, and lettuce), and 0.05 ppm for cereal forage, straw, and processed products		PMRA#s 1692335, 1692353, 1692343, 1692358, 1692371, and 1692378
	00649			0.02 ppm for barley and wheat grain, and 0.05 ppm for barley forage, straw, brewer's yeast, brewer's malt, brewer's grain, and malt sprouts; wheat forage, straw, and sprouts; and hops draff		
	00668			0.02 ppm in wheat and barley grain, 0.05 ppm in green materials of wheat and barley, straws of wheat and barley, wheat sprout, and orange fruit		
Livestock	00691	Fluoxastrobin (E and Z isomers) and the metabolite HEC7154		0.01 ppm for each analyte [fluoxastrobin (E and Z isomers) and HEC 7154] in milk, muscle and fat, and 0.02 ppm per analyte in liver and kidney.		PMRA#s 1692388, 1692402, and 1692394
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 Technical 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. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted

Study Type/Animal/PMRA #	Study Results
Acute Oral Standard test (401) Wistar rats PMRA # 1692408	**Low Toxicity** LD_{50} > 2000 mg/kg bw
Acute Oral Standard test (401) Wistar rats HEC 5725 N [90% E-isomer, 10% Z-isomer] PMRA # 1692412	**Low Toxicity** LD_{50} > 2000 mg/kg bw
Acute Dermal Wistar rats PMRA # 1692416	**Low Toxicity** LD_{50} > 2000 mg/kg bw
Inhalation (nose-only exposure) Wistar rats PMRA # 1692424	**Low Toxicity** LC_{50} > 4.998 mg/L Clinical signs included piloerection, ungroomed hair-coat, bradypnea, labored breathing pattern, nasal discharge, reduced motility, limp, mild hypothermia and decreased body weight. These clinical signs were resolved by Day 3.
Primary Eye Irritation NZW rabbits PMRA # 1692431	**Minimally irritating** MAS (24, 48 and 72 hrs) = 5.89/110
Primary Skin Irritation NZW rabbits PMRA # 1692422	**Non-irritating** MAS (24, 48 and 72 hrs) = 0/8
Skin Sensitization (Maximization Test of Magnusson and Kligman) Hartley guinea pigs PMRA # 1739247	**Unacceptable** Inappropriate dose selection for the topical and challenge phases.
Skin Sensitization (Maximization Test of Magnusson and Kligman)	**Not a dermal sensitizer**

Study Type/Animal/PMRA #	Study Results
Hartley guinea pigs PMRA # 1888362	
Metabolism/Toxicokinetics (single and repeated dose, oral, gavage) Wistar rats PMRA# 1692325 PMRA# 1692330 PMRA# 1692339 PMRA# 1692348 PMRA# 1692355 PMRA# 1692368	**Absorption and excretion:** HEC5725 was rapidly absorbed (80-92% of the administered dose (AD)) within 24 hrs of treatment, based on renal and biliary excretion from the single oral low dose bile-duct cannulation experiments in males. Plasma toxicokinetic data showed that the blood concentrations peaked at 0.17-0.38 hrs (T_{max}) in single low dose males and at 0.17 hrs in females, except in the study with [Pyrimidine-2-^{14}C] HEC5725 which produced a higher T_{max} of 8 hrs in males. In single high dose groups, T_{max} were 5.4 hrs in males and 8 hrs in females, while in single repeat dose animals, T_{max} was reached within 0.95 hrs in both sexes. The half-life of elimination ($t_{1/2}$ e) phase was biphasic for low ($t_{1/2}$e(1) = 0.88/0.72hrs ♂♀ and $t_{1/2}$e(2) = 10.50/10.90 hrs ♂♀) and high dose groups($t_{1/2}$e(1) = 2.32/40.09hrs ♂♀ and $t_{1/2}$e(2) = 6.98/6.84hrs ♂♀), and was similar between sexes, indicating that HEC5725 was partially subjected to an enterohepatic circulation. Plasma AUC were also similar between sexes, and were equal to 1.25-1.52 µg·h·mL and 54.10-61.30 µg·h·mL in the low and high dose groups, respectively, suggesting a saturation of the absorption in the high-dose groups. The majority of the fecal and urinary excretion occurred within the first 24 hrs and was nearly complete after 48 hrs. The predominant route of elimination was fecal via the bile. The biliary excretion accounted for 77-87% of the AD 24 hrs post-dosing in single oral low dose males. Fecal excretion accounted for 70-85% of the AD in low dose animals and 86-91% of the AD in high dose animals (both sexes). Urinary excretion resulted in the recovery of 12-20% of the AD in low dose groups and 10-15% of the AD in high dose animals (both sexes). After repeat dosing, the excretion pattern was similar to that following a single low dose. No significant levels of radioactivity were noted in expired air (≤ 0.24% of the AD). The overall recovery of administered radioactivity (urine, bile, feces, organs and tissues) ranged from 85-106% of the AD. **Distribution**: The distribution pattern of radioactivity was similar between sexes, and no significant differences were noted following a single low dose, single high dose or repeated low doses. The highest radioactive residues were observed in the liver, kidneys and urinary bladder. A high level of radioactive residues was noted in the wall and mucosa of the stomach with lower level in the lumen. Radioactivity was also observed in the blood, brown fat, perirenal fat, adrenal gland, skin, thyroid gland, pituitary gland and/or lung. Blood and brown fat had peak residual levels ≥ 0.1 µg/g and all other tissues had peak residual levels 0.093 and 0.033 µg/g. At 168 hrs, the radioactivity in all organs and tissues was low or below the limit of detection/quantification. Under the conditions of these studies, there was no evidence of bioaccumulation. **Metabolism**: HEC5725 was extensively metabolized. There were no significant differences in metabolism between dose groups and sexes. The parent compound was detected only in feces at 0.51-7.6% of the AD in low dose animals and 43-54% of the AD in high dose animals. The major metabolic route was hydroxylation and methoxylation of the parent compound followed by further conjugation with glucuronic acid. The second major route was the cleavage of the chlorophenyl moiety from the parent compound resulting in des-chlorophenyl metabolites. This metabolic route was not observed in the study with [Chlorophenyl-UL-^{14}C] HEC5725. The cleavage of the ether bridge between the pyrimidine ring and the methoxyiminotolyl ring of HEC5725, oxidative methylation and cleavage of the oximeter group and degradation metabolites were minor metabolic routes. The major urinary metabolites were HEC5725-E-des-chlorophenyl (1-4% of the AD), HEC5725-4-OH-pyrimidine-OH (1-2% of the AD), dioxazinyl-phenylketone (0.2-5% of the AD) and di-OH-diene-pyrimidine-OH-isomer 2 (1% of the AD). In feces, the major metabolites were HEC5725-di-OH-isomer 2 (5-13% of the AD), HEC5725-di-OH-dioxazine-OH-isomer 2 (2-12% of the AD), HEC5725-E-des-chlorophenyl (5-12% of the AD), HEC5725-des-

Study Type/Animal/PMRA #	Study Results
	chlorophenyl-dioxazine-OH (2-13% of the AD) and HEC5725-di-OH-dioxazine-OH-isomer 1 (5% of the AD). The major metabolites in bile-cannulated rats were E-des-chlorophenyl (10% of the AD), di-OH-GA and methoxy-OH-GA (8% of the AD), methoxy-OH-GA-dioxazine-OH (5-9% of the AD), des-chlorophenyl-dioxazine-OH (7% of the AD), oxime-GA (4% of the AD), dioxazinyl-phenylketone (4% of the AD), methoxy-OH-GA (1-3% of the AD), cysteine conjugates (2-4% of the AD) and benz-isoxazole (2% of the AD).
14-Day Oral Toxicity (diet) CD-1 mice Non-guideline PMRA # 1692452	**Effect levels were not established since this was a supplementary study.** **≥ 20.1/36.5 mg/kg bw/day:** ↑ GST; ↓ ALT, ↓ Leukocyte count, ↑ Proliferation index (periportal zones), ↑ Nuclear area of PCNA positive cells (periportal zones) ♂ **≥ 92.4/115.0 mg/kg bw/day:** ↑ ECOD, ↑ GLU-T, ↑ Proliferation index (periportal and perivenular zones) ♀ **354.0/571.0 mg/kg bw/day:** ↑ abs. and rel. liver wts; ↑ EROD, ↑ Aldrin Epoxide, ↑ epoxide hydrolase, ↓ ALT ♀
28-Day Oral Toxicity (diet) CD-1 mice Non-guideline PMRA # 1692466	**Effect levels were not established since this was a supplementary study** **≥ 81.1/135.1 mg/kg bw/day:** ↑ liver wts **≥ 313.4/439.2 mg/kg bw/day:** ↓ ALT activity **313.4/439.2 mg/kg bw/day:** ↑ hepatocelluar hypertrophy and cytoplasmic change ♂; ↑ hydropic degeneration ♀
28-Day Oral Toxicity Wistar rats PMRA # 1692440	**NOAEL = 11.7/10.6 mg/kg bw/day** **LOAEL = 63.6/54.6 mg/kg bw/day:** ↓ ALT; uniformly small cytoplasmic vacuolation of the adrenal cortex ♂ Hepatocyte proliferation index results: **1930.1/1441.3 mg/kg bw/day:** ↓ liver cell proliferation in both the perivenular ♂♀ and periportal ♂ zones Immunotoxic effects: **≥ 383.0/265.3 mg/kg bw/day:** ↓ bone marrow cell count ♂; ↓ IgA ♀
90-Day Oral Toxicity Wistar rats PMRA # 1692455	**NOAEL = 8.7/21.5 mg/kg bw/day** **LOAEL = 70.4/162.9 mg/kg bw/day:** ↓ bw, ↓ overall bwg, ↓ terminal bw, ↓ overall FC, ↓ spleen weight ♂; ↓ AST, ↓ ALT, ↓ ALD, ↓ ECOD, ↓ EROD, ↑ GST*, ↑ liver weight ♀ Immunotoxic effects **≥70.4/162.9 mg/kg bw/day:** ↓ IgG ♂ **Recovery groups** **580.0/1416.1 mg/kg bw/day:** ↓ bw, ↓ overall bwg, ↓ terminal bw, ↓ bilirubin ♂; 1 ♂ + 1 ♀ showed calculi formation, renal diffuse hyperplasia of the transitional epithelium, dilalation of the pelvis (♀ only) and inflammation of the urinary bladder (♂ only)

Study Type/Animal/PMRA #	Study Results
90-Day Oral Toxicity Beagle dogs PMRA # 1692476	**NOAEL = 3.0/3.0 mg/kg bw/day** **LOAEL = 24.8/24.2 mg/kg bw/day:** ↓ overall bwg, ↓ FC, ↑ AP, ↓ serum calcium, ↑ O-demethylase, ↑ cytochrome P450, ↑ UDP-GT or GLU-T, ↑ ECOD, ↑ ALD, ↑ EH, ↑ testosterone hydroxylases: 6β, 16α, 16β, 2β, ↑ liver weight, hepatocytomegaly; ↓ cholesterol, ↑ N-demethylase, ↑ kidney weight, degeneration of the proximal tubular epithelial cells of the kidneys, ↓ spleen weight ♂; ↓ bw, ↓ terminal bw, ↑ GST, ↑ pituitary gland weight, ↓ thymus weight ♀
90-Day Oral Toxicity Beagle dogs Non-guideline PMRA # 1692480	**Effect levels were not established since this was a supplementary study** **≥ 0.7/0.7 mg/kg bw/day:** ↑ liver weight ♂- abs&rel;♀- rel only; ↑ N-demethylase, ↑ O-demethylase, ↑ cytochrome P450 ♂ **1.4/1.5 mg/kg bw/day:** ↑ O-demethylase, ↑ AST at month 3 ♀ * Only two dose levels were used.
12-Month Oral Toxicity Beagle dogs PMRA # 1692486	**NOAEL = 1.7/1.5 mg/kg bw/day** **LOAEL = 8.1/7.7 mg/kg bw/day:** ↑ AP, ↑ liver weight, hepatocytomegaly; ↓ bw, ↓ overall bwg, ↓ terminal bw ♀
28-Day Dermal Toxicity Wistar rats PMRA # 1692489	**Systemic NOAEL = 1000 mg/kg bw/day** **Dermal irritation NOAEL = 1000 mg/kg bw/day** **1000 mg/kg bw/day:** ↑ thymus weight (♂: 9-16%; non-adverse)
18-Month Carcinogenicity Study (diet) CD-1 mice PMRA # 1692508	**NOAEL = 135.4/204.0 mg/kg bw/day** **LOAEL = 775.6/1265.1 mg/kg bw/day:** ↓ AST, ↓ ALT, ↑ liver weight; pallor appearance, liver hypertrophy, eosinophilic cytoplasmic changes in the liver ♀ **No evidence of carcinogenicity**
24-Month Oral Toxicity (diet) Wistar rats PMRA # 1692498	**NOAEL = 53.0 mg/kg bw/day in ♂, 35.2 mg/kg bw/day in ♀** **LOAEL = 181.3 mg/kg bw/day (♀):** ↓ bw (6-18%), ↓ overall bwg (10-32%), ↓ terminal bw (5-17%), ↓ FE, ↓ water intake, ↓ ALT, ↓ bilirubin, ↑ pH, ↓ urinary volume, ↓ urinary Ca concentration and total excretion, ↓ urinary P concentration and total excretion **271.9 mg/kg bw/day (♂):** ↑ rel kidney weights, discoloration of the kidneys, fatty changes in the liver, ↑ number of mast cells in the mesenteric lymph node ♂♀; ↓ bw (♂: 5-10%), ↓ overall bwg (13%), ↓ terminal bw (8%), ↓ ALT, ↓ bilirubin, ↑ pH, ↓ urinary P concentration and total excretion, kidney surface changes, kidney cysts, renal tubular dilation, renal glomerular dilation, arteritis/periarteritis of the kidneys ♂ Neoplastic lesions: malignant uterine adenocarcinomas (♀ terminal sac: 3-1-2-5-10 [20%], historical control range: 0-14%) **Tumours at a dose exceeding MTD; in females at 1083.2 mg/kg bw/d, bw decreased 9 – 19% and bwg decreased 23 – 32%; in males at 271.9 mg/kg bw/d, bw decreased 5 – 10% and bwg decreased 13%.**

Study Type/Animal/PMRA #	Study Results
2-Generation Dietary Reproductive Toxicity (diet) Wistar rats PMRA # 1692523	Parental Toxicity **NOAEL = 73.7/75.3 mg/kg bw/day** **LOAEL = 763.0/741.6 mg/kg bw/day:** ↓ bw, ↓ bwg, ↑ FC, ↓ terminal bw, ↑ liver weight Offspring Toxicity **NOAEL = 75.3 mg/kg bw/day** **LOAEL = 741.6 mg/kg bw/day:** ↓ bw, ↓ bwg, delay in preputial separation (F_1: 2.6 days), ↓ terminal bw ↓ thymus weight (non-adverse), ↓ spleen weight (non-adverse), incomplete ossification of the calvarium (F_1: 0 [0]-3 [2]-0 [0]-11 [9]) Reproductive Toxicity **NOAEL = 741.6 mg/kg bw/day** There were no treatment-related effects on the Ca and P content in the femurs of F_1 pups. **No sensitivity of the young**
Oral Developmental Toxicity (gavage) Wistar rats PMRA #1692526	Maternal Toxicity **NOAEL = 1000 mg/kg bw/day** **1000 mg/kg bw/day:** ↑ liver weight (non-adverse), lymphoid cell foci in the liver (non-adverse) Developmental Toxicity **NOAEL = 1000 mg/kg bw/day** **No sensitivity of the young**
Oral Developmental Toxicity (gavage) – range finding study NZW rabbits PMRA # 1692527 Effects were not established since this was a supplementary study	**Effect levels were not established since this was a supplementary study** (full study was not submitted to the PMRA; reported effects are summarized below) Maternal Toxicity **≥ 100 mg/kg bw/day:** body weight loss, soft feces from GD 1-3, light colored feces **300 mg/kg bw/day:** one abortion on GD 22 (distinct liver lobulation at necropsy) **1000 mg/kg bw/day:** ↓ bwg, ↓ FC, ↓ urination, ↓ water intake, ↓ amount of feces, ↓ placental weights, ↑ incidence of coarse grained placentas, placenta infiltrated with punctiform black vesicles was observed in one dam, one dams showed early delivery, two dams were cold to touch Developmental Toxicity **1000 mg/kg bw/day:** ↓ fetal weights, black punctiform vesicles in the liver, distinct liver lobulation, arthrogryposis, cleft palate
Oral Developmental Toxicity (gavage) NZW rabbits PMRA # 1692527	Maternal Toxicity **NOAEL = 100 mg/kg bw/day** **400 mg/kg bw/day:** ↓ bwg from GD 6-9, bw loss from GD 6-9, ↓ FC from GD 6-9 Developmental Toxicity **NOAEL = 400 mg/kg bw/day** **No sensitivity of the young**

Study Type/Animal/PMRA #	Study Results
Acute Neurotoxicity (gavage) Wistar rats PMRA # 1692530	**NOAEL = 2000 mg/kg bw/day** No treatment-related effects on mortality, clinical signs, body weights, brain weights, gross pathology or neuropathology. **No evidence of neurotoxicity**
90-Day Neurotoxicity (diet) Wistar rats PMRA # 1692468	**NOAEL = 59.5/71.7 mg/kg bw/day** **473.9/582.4 mg/kg bw/day:** ↓ bw, ↓ overall bwg, ↓ terminal bw, ↑ rel brain weight (non-adverse) **No evidence of neurotoxicity**
Gene mutations in bacteria (Ames test) PMRA # 1692491	**Negative** Tested up to limit, insoluble and cytotoxic concentrations.
Gene mutations in bacteria (Ames test) HEC 5725 N [90% E-isomer, 10% Z-isomer] PMRA # 1692494	**Negative** Tested up to limit and insoluble concentrations.
Gene mutations in mammalian cells in vitro PMRA # 1692493 PMRA # 1692496	**Negative in two studies** Tested up to cytotoxic and insoluble concentrations.
Chromosome aberrations in vitro PMRA # 1692492	**Unacceptable** Precipitation and cytotoxicity observed at low doses (20 or 40 µg/mL ± S9) could interfere with the assessment of the clastogenicity potential of HEC 5725. This study is of poor quality.
Micronucleus assay in vivo (intraperitoneal injection) NMRI mice PMRA # 1692518	**Negative** **≥ 75 mg/kg bw/day:** Clinical signs including apathy, roughened fur, weight loss, sternal recumbency, spasm, shivering, difficulty in breathing and slitted eyes were observed until sacrifice.
60-Day Oral Toxicity (dietary) Wistar rats Non-guideline PMRA # 1692532	**Effect levels were not established since this was a supplementary study** **≥ 59.7/146.3 mg/kg bw/day:** ↓ serum S-bile acid; ↑ serum citric acid, ↑ pH, ↓ total urinary P excretion, ↑ urinary Ca concentration and total excretion, ↑ total urinary oxalic acid excretion, ↑ ratio Ca/creatinine clearance, CaOx crystal formation with ↑ severity, ↑ bacteria count, uniformly small cytoplasmic vacuolation ♂ **520.3/1544.2 mg/kg bw/day:** ↑ FC, ↓ overall FE, ↑ plasma Ca, ↑ unbound plasma Ca; ↓ bw, ↓ bwg, ↓ terminal bw, ↑ serum citric acid, ↑ pH, ↓ total urinary P excretion, ↓ total urinary creatinine excretion, ↑ ratio Ca/creatinine clearance, CaOx crystal formation ♀ **1% NH_4Cl vs 1% NH_4Cl+476.5/1590.6 mg/kg bw/day HEC 5725 group:** **520.3/1544.2 mg/kg bw/day:** ↑ FC, ↑ serum citric acid, ↓ total urinary P excretion, ↑ ratio Ca/creatinine clearance, CaOx crystal formation with ↑ severity, ↑ pH; uniformly small

Study Type/Animal/PMRA #	Study Results
	cytoplasmic vacuolation of the adrenal cortex, ↑ plasma Ca, ↑ unbound plasma Ca, ↑ urinary Ca concentration and total excretion, ↑ total urinary Mg excretion, ↑ total urinary Cl excretion ♂; ↓ bw, bwg, ↓ overall FE, ↓ unbound plasma Ca, ↓ total urinary creatinine excretion, ↓ total urinary urea excretion ♀ **Conclusion:** When animals were given a substance that decreased urinary pH, there was a decreased incidence of calcium oxalate crystal formation in males treated with high-doses of HEC 5725. Co-treatment with 1% NH_4Cl and HEC 5725 maintained the urinary pH at similar level as that of the main control animals and did not result in decreased serum and urinary calcium levels or complete recovery of calcium oxalate crystal formation in high-dose males, suggesting that the effects above were due to HEC 5725-induced pH changes. In summary, the major urinalysis changes observed in this study, including decreased total urinary excretion of phosphorus, increased serum and urinary calcium levels and increased pH noted in males at ≥ 59.7 mg/kg bw/day and in high-dose females most likely explained the formation of calcium oxalate crystals in urine, which may lead to stone formation and corresponding urinary tract lesions observed in the previous subchronic rat dietary study. Ophthalmoscopic examination, hematology analysis, liver, heart, spleen, thymus, testis, epididymis, ovary and uterus weights and their corresponding histopathology were not assessed.
28-Day Oral Toxicity Wistar rats HEC 5725 N [90% E-isomer, 10% Z-isomer] PMRA # 1692444	**NOAEL = 9.7 mg/kg bw/day in ♂, not established in ♀** **LOAEL = 49.9/43.4 mg/kg bw/day**: ↓ N-demethylase (♂: 28-50%; ♀: 13-24%); ↓ ALT, ↓ AP (no dose-response), ↑ total urinary Ca excretion ♂ No clear treatment-related immunotoxic effects were observed.
28-Day Oral Toxicity Wistar rats HEC 5725 [98.8% E-isomer, 1.2% Z-isomer] HEC 5725 A [62.5% E-isomer, 35.2% Z-isomer] PMRA # 1692450	**HEC 5725:** **NOAEL = 41.5/52.7 mg/kg bw/day** **LOAEL = 209.7/261.2 mg/kg bw/day:** ↓ AST; ↓ triglycerides, ↑ urinary calcium levels, ↓ prostate weight ♂; ↑ urea, ↓ N-DEM, adrenal cytomegaly ♀ **HEC 5725 A:** **NOAEL = 42.1/47.7 mg/kg bw/day** **LOAEL = 226.6/247.6 mg/kg bw/day:** ↓ AST ♂♀; ↓ ALT, ↓ N-DEM, adrenal cytomegaly ♀ The studies allow for comparison between HEC 5725 and HEC 5725 A; however the endpoint selection should not be based on the data due to the instability of HEC 5725 A.
5-Week Immunotoxicity (PFC assay) CD-1 mice PMRA # 1692529	**Unacceptable** Large reporting gaps and lack of adequate information provided to interpret results of PFC assay. - Uncertainty in diet preparation, concentration and/or stability - Lack of details on the conduct of the PFC assay (example, necropsy and spleen/thymus weights were not reported) - High variability within each study group Absence of positive control

Study Type/Animal/PMRA #	Study Results
Metabolism study (non-guideline) Wistar rats PMRA # 1692539	Pretreatment observations: **8000 ppm:** ↓ bw (♂: 5-7%), ↓ overall bwg (♂: 23%), ↑ FC (7-39%) Pharmacokinetic results: 48 hrs following [^{33}P]orthophosphate administration, 3.47% AD and 0.37% AD were excreted via urine of untreated and HEC 5725-treated males, respectively. The total amount of radioactivity excreted in feces and GIT (amount of unabsorbed [^{33}P]) accounted for 22.4% AD in untreated and 27.6% AD in HEC 5725-treated animals. A significant decrease in urinary phosphorus excretion was observed in animals treated with HEC 5725 (↓89%) compared to untreated animals. This reduction was accompanied with decreased phosphorus absorption (unabsorbed portion was ↑23% compared to untreated animals) and reduced phosphorus uptake in the bone (↓11%), suggesting that decreased phosphorus absorption was counter-regulated by decreased urinary phosphorus excretion. Excretion of [^{45}Ca] in urine accounted for 0.55% AD in untreated group and for 2.78% AD in HEC 5725-treated group following 48 hrs of [^{45}Ca] chloride administration. The total amount of radioactivity excreted in feces and GIT (amount of unabsorbed [^{45}Ca]) accounted for 31.5% AD in untreated and 30.8% AD in HEC 5725-treated animals. Urinary calcium levels were significantly increased in HEC 5725-treated males (↑407%) compared to untreated males, while the fraction of unabsorbed calcium and calcium uptake in the bone were not significantly different between HEC 5725-treated and untreated animals. Increased urinary calcium levels observed in this study were most likely due to the reduction of tubular calcium reabsorption and attributed to decreased phosphorus absorption. The effects of HEC 5725 on phosphorus and calcium levels observed in this study were consistent with the 90-day rat dietary study (PMRA # 1692455) and the 2-month dietary rat study (PMRA # 1692532), and supported that altered phosphorus and calcium homeostasis was attributed to reduced phosphorus absorption.

Metabolite data HEC 5725-E-des-chlorophenyl

Gene mutations in bacteria (Ames test) PMRA # 1692544	**Negative** Tested up to limit and cytotoxic concentrations.
Gene mutations in mammalian cells in vitro PMRA # 1692546	**Negative** Tested up to limit and cytotoxic concentrations.
Chromosome aberrations in vitro PMRA # 1692545	**Equivocal** Tested up to limit and cytotoxic concentrations. A statistically significant increase in the number of metaphases with aberrations (including [3.3-fold] and excluding gaps [3.2-fold]) was observed at 3500 µg/mL without S9 compared to control. Based on the evidence of a dose-response relationship, reproducibility of the replicate cultures, values being statistically and significantly higher compared to concurrent controls, values being above the range of historical control data, but the aberrations occurred in the presence of cytotoxicity (associated with a 42.4% reduction in relative mitotic index), these findings were considered to be equivocal.

Table 3 Toxicity Profile of End-use Product Evito 480 SC Fungicide

(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 #	Study Results
Acute Oral Up/Down Test (425) Wistar rats PMRA #1737111	**Low Toxicity** LD_{50} > 5000 mg/kg bw Clinical signs included loose stool, red stain – chin, greenish discharge – perianal area, yellow stain – perianal area and wetness – perianal area. All signs had abated by day 2.
Acute Dermal Wistar rats PMRA #1737112	**Low Toxicity** LD_{50} > 5000 mg/kg bw Clinical signs included red staining and discharge around eyes and/or nose. All clinical signs had abated by day 3.
Acute Inhalation Wistar rats PMRA #1737113	**Low Toxicity** LC_{50} > 2.17 mg/L Clinical signs included ungroomed coat, piloerection, bradypnea, laboured breathing patterns, nostril reddening, reduced motility, limp, high-legged gait and hypothermia. All clinical signs had abated by day 1.
Primary Eye Irritation NZW rabbits PMRA #1737114	**Non-irritating** MAS (24, 48, 72 hrs) = 0/110
Primary Dermal Irritation NZW rabbits PMRA #1737115	**Slightly irritating** MAS (24, 48, 72 hrs) = 1.4/8
Dermal Sensitization Hartley albino guinea pigs PMRA #1737116	**POTENTIAL SKIN SENSITIZER**

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Fluoxastrobin Technical Fungicide

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary general population	Not required.		
Repeated dietary	1-year dog dietary study	NOAEL = 1.5 mg/kg bw/day Decreased body weights, increased liver enzymes, increased liver weights assoc. with hepatocytomegaly	100

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
	ADI = 0.015 mg/kg bw/day		
Short and Intermediate-term dermal	21-day rat dermal toxicity study	NOAEL: 1000 mg/kg bw/day No findings	100
Short-and Intermediate-term inhalation[2]	90-day dog dietary study	NOAEL = 3 mg/kg bw/day Decreased body weights, increased liver enzymes, decreased serum calcium, decreased cholesterol (♂), increased kidney weights and degeneration (♂), decreased spleen weights (♂), increased pituitary weights (♀) and decreased thymus weights (♀)	100
Non-dietary oral ingestion (short-term)	90-day dog dietary study	NOAEL = 3 mg/kg bw/day Decreased body weights, increased liver enzymes, decreased serum calcium, decreased cholesterol (♂), increased kidney weights and degeneration (♂), decreased spleen weights (♂), increased pituitary weights (♀) and decreased thymus weights (♀)	100
Cancer	Not required.		

Table 5 Integrated Food Residue Chemistry Summary

Direction for Use						
Crop	**Max Applic. #/ Season**	**Rate (g a.i./ha/application)**	**Crop Growth Stage**	**PHI (days)**	**RTI (days)**	**Total Rate (g a.i./season)**
Wheat (spring and durum), barley	2	70-140	Zadok's 30 to 59	Forage: 7 Grain: 40	14-21	280
Corn (field, seed)	2	70-142	Not provided	30	7-10	284
Sweet corn	4		Not provided	7		568
Soybean	2	70-142	No later than full seed (R6)	Not provided	14	284
Potato	6	133	Not provided	7	7-10	800
Tomato and pepper	4	133	Not provided	3	7-10	532
Imported Celery*	4	200	Not provided	3	7-10	800
Strawberry	4	70-134	Not provided	0	14-21	536
* Registered in the US.						

Physicochemical Properties	
Melting point or range	103-108 °C
Specific gravity at 20 °C	1.422
Water solubility at 20°C, pH 7.0	2.29 mg/L
Vapour pressure	6×10^{-7} mPa at 20 °C
Octanol/water partition coefficient Log(K_{ow}) at 20 °C	log K_{ow} = 2.86 @ 20°C

Analytical Methodology	
Parameters	**Plant Matrices**
Method ID	Method 00604
Type	LC-MS/MS
Analytes	Fluoxastrobin (sum of E and Z isomers)
LOQ	0.01 ppm for potato tuber, 0.02 ppm for cereal grain, tomato, cucumber, onion and lettuce, 0.05 ppm for cereal forage, straw and processed commodities.
Standard	External
ILV	The method was successfully validated in peanut nutmeat (LOQ of 0.01 ppm) by an independent laboratory with modification to include the use of internal standard.

Direction for Use	
Extraction/clean-up	Extracted by methanol/water (4/1, v/v) using accelerated solvent extraction, followed by passing through a C_{18} SPE column.
Method ID	Method 00649
Type	LC-MS/MS
Analytes	Fluoxastrobin (sum of E and Z isomers)
LOQ	0.02 ppm for barley and wheat grain, and 0.05 ppm for barley forage, straw, brewer's yeast, brewer's malt, brewer's grain, and malt sprouts; wheat forage, straw, and sprouts; and hops draff.
Standard	External
ILV	The method was successfully validated in wheat grain (LOQ of 0.01 ppm) by an independent laboratory
Extraction/clean-up	Extracted by acetonitrile/water (3/1, v/v) using conventional procedure or microwave extraction, followed by passing through a C_{18} SPE column.
Method ID	Method 00668
Type	LC-MS/MS
Analytes	Fluoxastrobin (sum of E and Z isomers)
LOQ	0.02 ppm in wheat and barley grain, 0.05 ppm in other matrices (forage, straw and orange)
Standard	External
ILV	The method was successfully validated by an independent laboratory
Extraction/clean-up	Extracted by acetonitrile/water (3/1, v/v), followed by passing through a C_{18} SPE column.
Multiresidue method	MRM is not suitable for analysis of fluoxastrobin and the metabolite HEC7154.
	Animal Matrices
Method ID	Method 00691
Type	LC-MS/MS
Analytes	Fluoxastrobin (sum of E and Z isomers) and the metabolite HEC 7154
LOQ	0.01 ppm/analyte in milk, muscle and fat, 0.02 ppm/analyte in liver and kidney.
Standard	External
ILV	The method was successfully validated by an independent laboratory
Extraction/clean-up	Extracted by acetonitrile/water (4/1, v/v; use acetonitrile/water/hexane, 4/1/5, v/v/v for extraction of fat sample), followed by centrifugation and SPE clean-up.

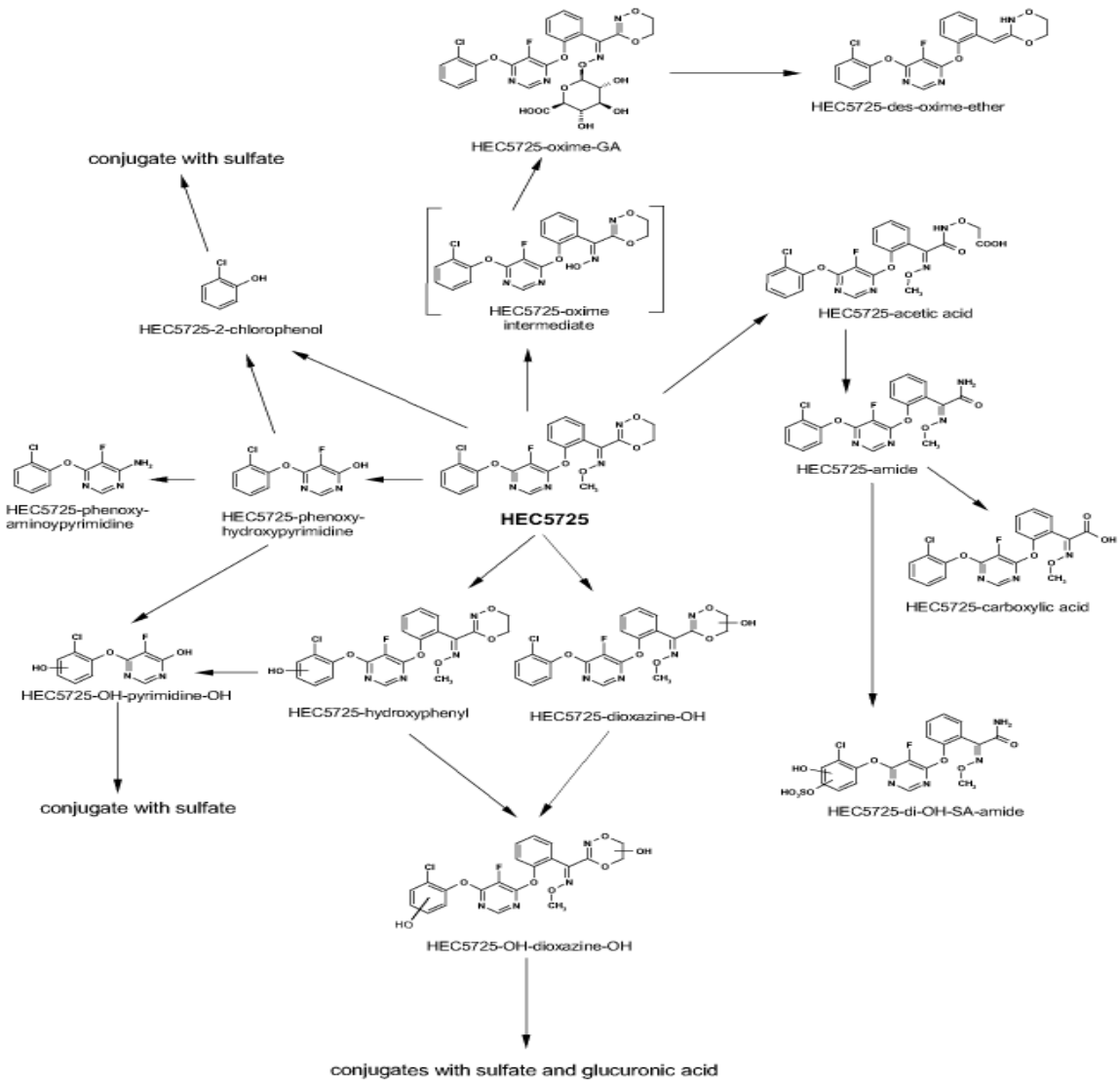
NATURE OF THE RESIDUE IN ANIMALS – Laying Hen	**PMRA# 1893592**
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C] and [Chlorophenyl-UL -14C] Fluoxastrobin**

Laying hens (two groups with 6 birds in each group) were dosed orally once daily with either [Methoxyiminotolyl-ring-UL-14C] and [Chlorophenyl-UL -14C] fluoxastrobin at a rate of 187/198 ppm in the feed for 3 consecutive days. Samples of excreta were collected daily. Samples of eggs were collected twice daily. The samples of liver, muscle and fat were collected at sacrifice.

Matrices	[Methoxyiminotolyl-ring-UL-14C]		[Chlorophenyl-UL -14C]	
	TRRs (ppm)	% AD	TRRs (ppm)	% AD
Excreta (Total)	-	72.5	-	72.2
Eggs (Day 3)	0.84	0.061	0.35	0.029
Muscle	0.53	-	0.38	-
Fat (subcutaneous)	0.90	-	0.68	-
Liver	9.5	-	8.1	-
Kidney	6.2	-	5.0	-
Eggs from ovary/oviduct	4.0	-	2.6	-
Skin without subcutaneous fat	1.1	-	1.0	-
Total % AD	75.9		74.1	

Direction for Use				
Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[Methoxyiminotolyl -14C]**	**[Chlorophenyl-14C]**	**[Methoxyiminotolyl -14C]**	**[Chlorophenyl-14C]**
Eggs	Fluoxastrobin (E isomer), HEC5725-salicylic acid (12% TRRs, 0.039 ppm)	Fluoxastrobin (E isomer), HEC5725-2-chlorophenol, HEC5725-phenoxyhydroxy-pyrimidine	Fluoxastrobin (Z isomer), and 8 other metabolites, no single metabolite was more than 3.3% TRRs, or 0.010 ppm.	Fluoxastrobin (Z isomer), and 9 other metabolites, no single metabolite was more than 8.9% TRRs, or 0.011 ppm.
Liver	None	HEC5725-2-chlorophenol, HEC5725-phenoxyhydroxy-pyrimidine	Fluoxastrobin (E isomer), and 16 other metabolites, no single metabolite was more than 7.4% TRRs, or 0.703 ppm.	Fluoxastrobin (E isomer), and 20 other metabolites, no single metabolite was more than 3.7% TRRs, or 0.297 ppm.
Muscle	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer), HEC5725-phenoxyhydroxy-pyrimidine	Fluoxastrobin (Z isomer), and 14 other metabolites, no single metabolite was more than 6.2% TRRs, or 0.033 ppm.	Fluoxastrobin (Z isomer), and 12 other metabolites, no single metabolite was more than 8.0% TRRs, or 0.30 ppm.
Fat	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer), HEC5725-phenoxyhydroxy-pyrimidine	Fluoxastrobin (Z isomer), and 11 other metabolites, no single metabolite was more than 7.3% TRRs, or 0.066 ppm.	Fluoxastrobin (Z isomer), and 8 other metabolites, no single metabolite was more than 2.6% TRRs, or 0.018 ppm.

Direction for Use
Proposed metabolic scheme in hens:



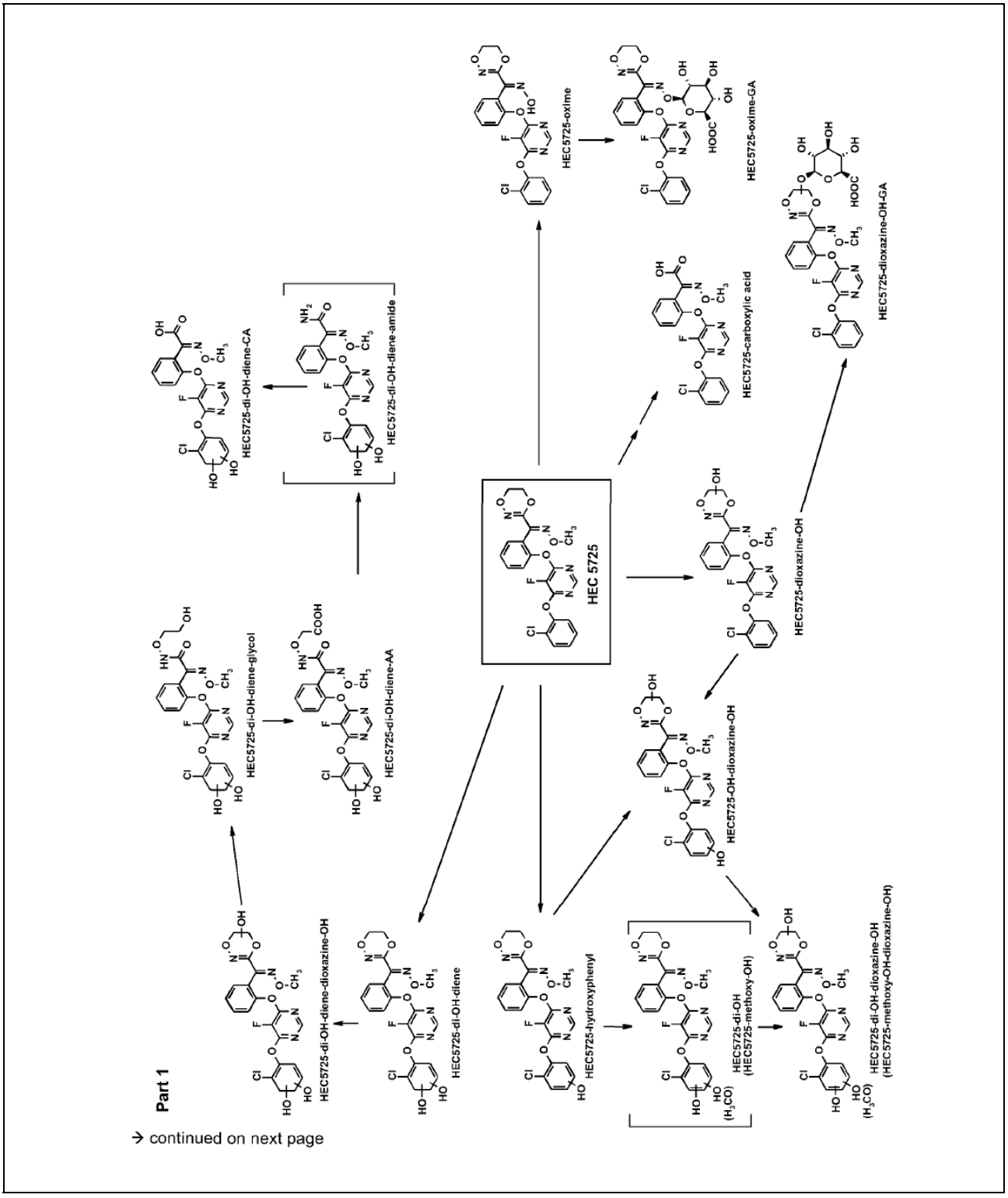
Fluoxastrobin is metabolized in hens via:

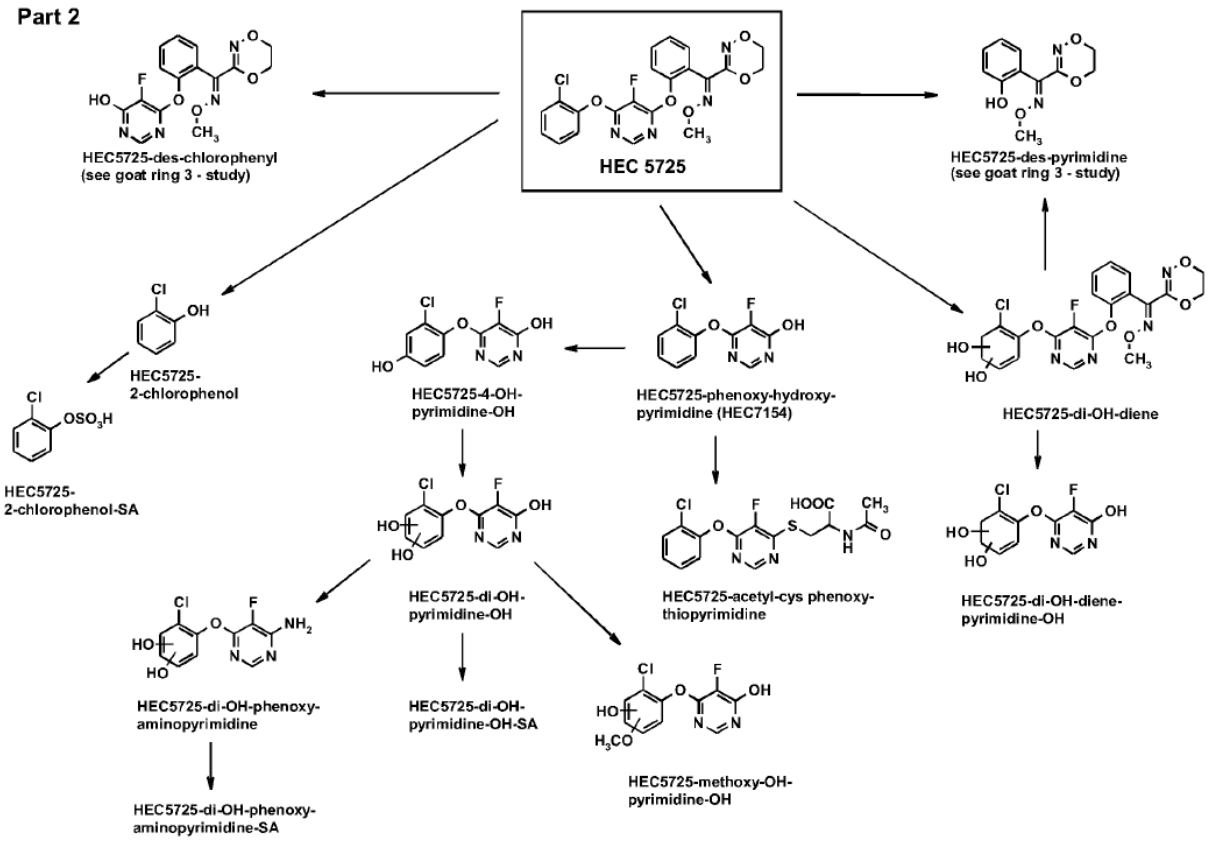
i. hydroxylation of the chlorophenyl ring to mono- and dihydroxy isomers;
ii. hydroxylation of the dioxazine ring followed by oxidative ring opening and further degradation of dioxazine ring;
iii. oxidative demethylation of the oximether group and cleavage of this group;
iv. cleavage of the ether group in the pyrimidine moiety to 2-chlorophenol and HEC5725-phenoxyhydroxy-pyrimidine; or to methoxyiminotolyl-dioxazine ring and methoxy iminotolyl ring metabolites, and
v. conjugation of the hydroxyl groups to glucuronic acid and sulphate conjugate.

NATURE OF THE RESIDUE IN ANIMALS - GOAT		**PMRA# 1893593**
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C] and [Chlorophenyl-UL -14C] Fluoxastrobin**	
Lactating goats (one animal for each treatment) were dosed orally once daily with either [Methoxyiminotolyl-ring-UL-14C] or [Chlorophenyl-UL -14C] fluoxastrobin at a rate of 180/265 ppm in the feed for 3 consecutive days. Samples of excreta were collected daily. Milk was collected twice daily before each dosing throughout the study and tissues (muscle, fat, liver and kidney) were collected at sacrifice.		
Matrices	[[Methoxyiminotolyl-ring-UL-14C]	[Chlorophenyl-UL -14C]

Direction for Use				
	TRRs (ppm)	% AD	TRRs (ppm)	% AD
Urine (Total)	-	17.458	-	11.749
Feces (Total)		45.049	-	44.131
Milk (Day 3)	0.197	0.0107	0.4246	0.0141
Muscle	0.247	0.254	0.503	0.503
Fat	0.580	0.226	0.375	0.149
Kidney	2.630	0.033	3.948	0.034
Liver	8.301	0.767	18.232	1.048
Total % of AD	63.849		57.717	
Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[Methoxyiminotolyl-14C]**	**[Chlorophenyl-14C]**	**[Methoxyiminotolyl-14C]**	**[Chlorophenyl-14C]**
Evening milk	HEC5725-2-cyanophenol-SA	HEC5725-phenoxy-hydroxypyrimidine, HEC5725-di-OH-diene-pyrimidine-OH(isomer 1), HEC5725-di-OH-diene-pyrimidine-OH(isomer 2), HEC5725-2 chlorophenol-SA	Fluoxastrobin (E isomer), and 16 other metabolites, no single metabolite was more than 6.94% TRRs, or 0.015 ppm.	Fluoxastrobin (E isomer), and 5 other metabolites, no single metabolite was more than 5.71% TRRs, or 0.019 ppm.
Muscle	HEC5725-benz-isoxazole	HEC5725-phenoxy-hydroxypyrimidine	Fluoxastrobin (E isomer), and 17 other metabolites, no single metabolite was more than 5.12% TRRs, or 0.013 ppm.	Fluoxastrobin (E isomer), and 7 other metabolites, no single metabolite was more than 7.31% TRRs, or 0.035 ppm.
Fat	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer), HEC5725-hydroxyphenyl, HEC5725-phenoxy-hydroxypyrimidine	17 other metabolites, no single metabolite was more than 7.05% TRRs, or 0.041 ppm.	Fluoxastrobin (Z isomer), HEC5725-di-OH-diene (isomer 2), HEC5725-di-OH - diene-dioxazine-OH
Liver	HEC5725-dioxazinyl-alcohol derivative	HEC5725-hydroxyphenyl	Fluoxastrobin (E isomer) and 16 other metabolites, no single metabolite was more than 9.23% TRRs, or 0.766 ppm.	Fluoxastrobin (E and Z isomers), and 14 other metabolites, no single metabolite was more than 8.29% TRRs, or 1.511 ppm.
Kidney	HEC5725-2-cyanophenol-SA	HEC5725-phenoxy-hydroxypyrimidine	Fluoxastrobin and 13 other metabolites, no single metabolite was more than 9.04% TRRs, or 0.238 ppm.	Fluoxastrobin (E isomer), and 12 other metabolites, no single metabolite was more than 5.59% TRRs, or 0.221 ppm.

Proposed metabolic scheme in goats:





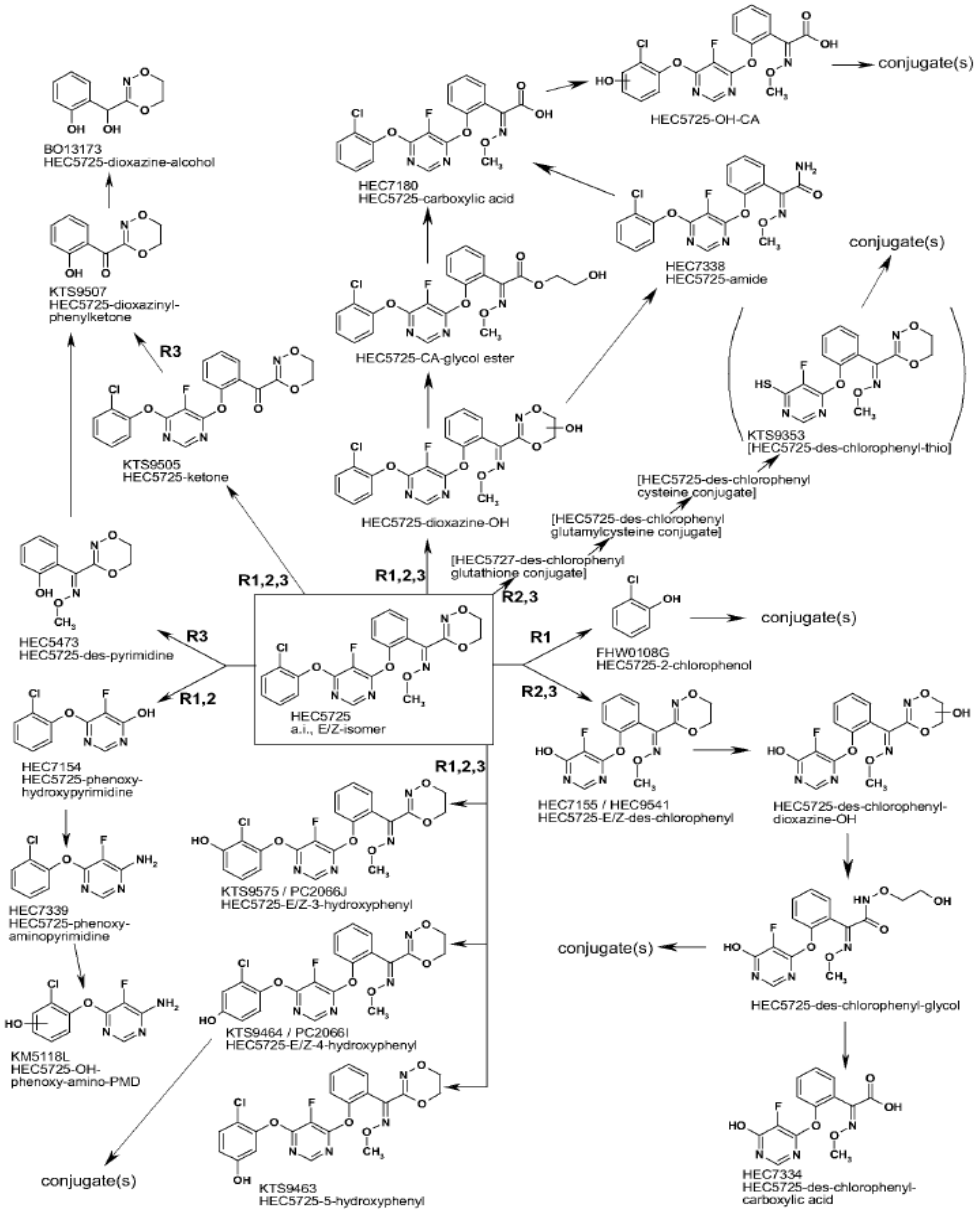
The principal metabolic reactions were:
• hydroxylation of the chlorophenyl ring to monohydroxy and dihydroxy isomers,
• bis hydroxylation and reduction of the chlorophenyl ring to dihydroxy diene isomers,
• hydroxylation of the dioxazine ring followed by oxidative ring opening and further degradation of the dioxazine ring,
• cleavage of the ether group in the pyrimidine moiety to 2-chlorophenol and HEC5725-des-chlorophenyl (see first goat metabolism study),
• cleavage of the ether group in the pyrimidine moiety to HEC5725-phenoxy-hydroxypyrimidine and HEC5725-des-pyrimidine (see first goat metabolism study) and derivatives thereof,
• oxidative demethylation of the oximether group,
• bis hydroxylation and reduction of the clorophenyl ring of HEC5725-phenoxyhydroxypyrimidine to dihydroxy diene isomers and
• conjugation of free hydroxyl groups to give glucuronic acid and sulfate conjugates.

NATURE OF THE RESIDUE IN PLANTS - Wheat	**PMRA# 1692337, 1692345 and 1692363**
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C], [Chlorophenyl-UL -14C], and [Pyrimidine-2-14C] Fluoxastrobin**
Test site	Outdoors
Treatment	Seed treatment and foliar spray
Rate	Seed treatment on the day of planting and two foliar applications for each label. Two foliar treatments at ~300 g a.i.ha/application.
Timing	First application: BBCH 32 growth stage. Second application: BBCH 69 growth stage.
Preharvest interval	Immature forage: 14-36 days after the planting, received no foliar application. Hay: 9-10 days after 2nd application. Straw and grain: 47-63 days after 2nd application.
End-use product	Formulated as a emulsifiable concentrate

TRRs in Wheat Raw Agriculture Commodities			
Matrix	[Methoxyiminotolyl-ring-UL-14C]	[Chlorophenyl-UL -14C]	[Pyrimidine-2-14C]
Wheat Forage	0.02	0.06	0.05
Wheat hay	55.67	9.71	40.07
Wheat straw	79.95	78.14	74.68
Wheat grain	0.71	0.53	0.57

Metabolite Identified	**Major metabolites (>10% TRRs)**	**Minor metabolites (<10% TRRs)**
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C]**	
Wheat Forage	Fluoxastrobin (E isomer), HEC5725-E-4-OH-Glc-MA	HEC5725-E-4-OH-Glc
Wheat hay	Fluoxastrobin (E and Z isomers)	25 other metabolites, no single metabolite was more than 1.2% TRRs, or 0.68 ppm.
Wheat straw	Fluoxastrobin (E and Z isomers)	32 other metabolites, no single metabolite was more than 2.4% TRRs, or 1.96 ppm.
Wheat grain	Fluoxastrobin (E and Z isomers)	4 other metabolites, no single metabolite was more than 5.0% TRRs, or 0.04 ppm.
Metabolite Identified	**Major metabolites (>10% TRRs)**	**Minor metabolites (<10% TRRs)**
Radiolabel Position	**[Chlorophenyl-UL -14C]**	
Wheat Forage	Fluoxastrobin (E isomer)	Fluoxastrobin (Z isomer), HEC5725-2-chlorophenol-Glc, HEC5725-E-4-OH-Glc-MA, HEC5725-amide
Wheat hay	Fluoxastrobin (E and Z isomers)	13 other metabolites, no single metabolite was more than 2.2% TRRs, or 0.22 ppm.
Wheat straw	Fluoxastrobin (E and Z isomers)	17 other metabolites, no single metabolite was more than 2.7% TRRs, or 2.10 ppm.
Wheat grain	Fluoxastrobin (E and Z isomers)	5 other metabolites, no single metabolite was more than 2.4% TRRs, or 0.01 ppm.
Metabolite Identified	**Major metabolites (>10% TRRs)**	**Minor metabolites (<10% TRRs)**
Radiolabel Position	**[Pyrimidine-2 -14C]**	
Wheat Forage	Fluoxastrobin (E isomer), HEC5725-E-4-OH-Glc-MA	HEC5725-E-4-OH-Glc
Wheat hay	Fluoxastrobin (E and Z isomers)	25 other metabolites, no single metabolite was more than 1.2% TRRs, or 0.68 ppm.
Wheat straw	Fluoxastrobin (E and Z isomers)	29 other metabolites, no single metabolite was more than 2.4% TRRs, or 1.79 ppm.
Wheat grain	Fluoxastrobin (E and Z isomers), Glucose	7 other metabolites, no single metabolite was more than 6.7% TRRs, or 0.04 ppm.

Proposed metabolic scheme in wheat:



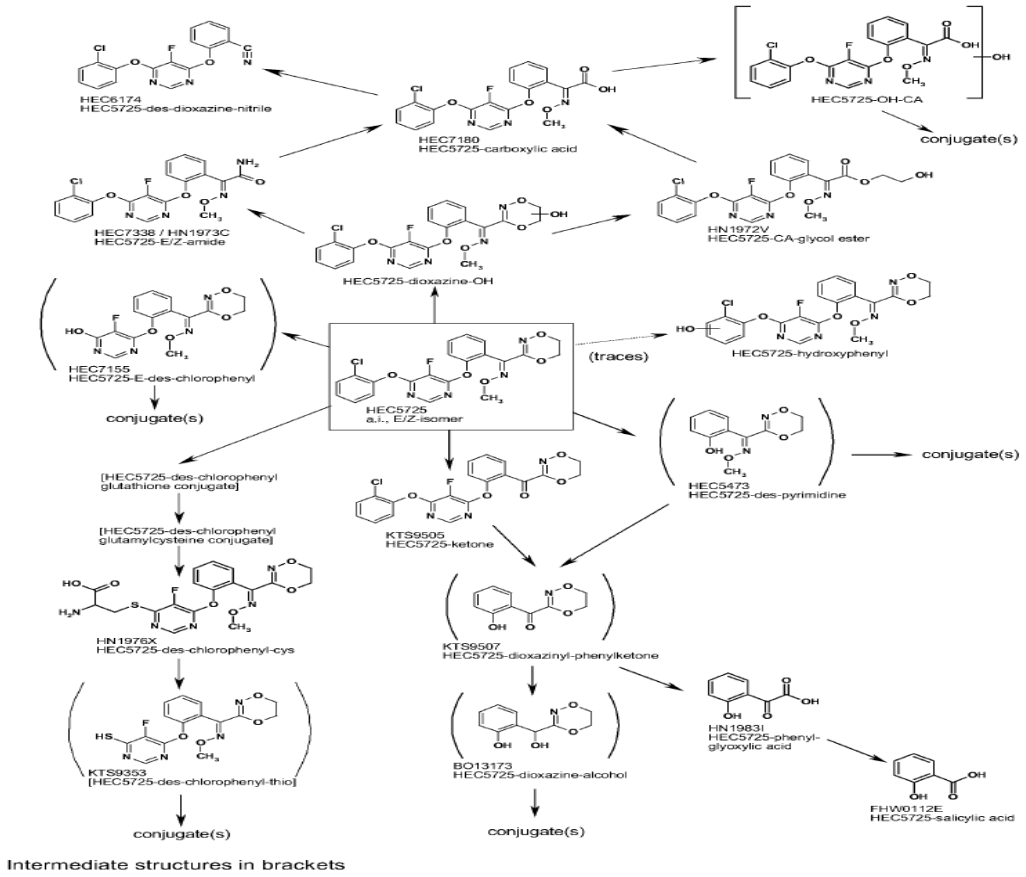
Note: Rx refers to a study using a certain radiolabelling position study: R1 = ring 1 label [2], R2 = ring 2 label, [3], R3 = ring 3 label (present study).

Fluoxastrobin is metabolized in wheat via the following, or combinations of the following, reactions:

(i) isomerization of the oximether to form the Z-isomer of fluoxastrobin;
(ii) hydroxylation of the chlorophenyl ring to monohydroxy isomers;
(iii) oxidative ring opening and degradation of the dioxazine ring;
(iv) cleavage of the oximether;
(v) cleavage of the parent molecule to form HEC5725-deschlorophenyl, and to a lesser extent HEC5725-E-des-pyrimidine;
(vi) nucleophilic substitution of the chlorophenol ring by glutathione, followed by stepwise degradation of the HEC5725-deschlorophenyl-glutathione to HEC5725-des-chlorophenyl-thio; and
(vii) conjugation of hydroxyl and thiol groups to glucosyl, glucosyl-malonyl, glucosyl-sulfate, and malonyl conjugates.

NATURE OF THE RESIDUE IN PLANTS - Peanut		**PMRA# 1692377 and 1692387**
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C] and [Pyrimidine-2-14C] Fluoxastrobin**	
Test site	Greenhouse	
Treatment	Foliar spray	
Rate	Three applications for each label. Foliar applications at ~250 g a.i./ha/application	
Timing	1st application: BBCH 66 growth stage, 2nd application: BBCH 79 growth stage, 3rd application: BBCH 89 growth stage,	
Preharvest interval	Peanut hay and nutmeat: 14 days after the last application, dried 4 days prior to collection.	
End-use product	Formulated as a emulsifiable concentrate	
TRRs in Peanut Raw Agriculture Commodities		
Matrix	[Methoxyiminotolyl-ring-UL-14C] (ppm)	[Pyrimidine-2-14C] (ppm)
Peanut hay	141.82	129.86
Nutmeat	0.055	0.146
Metabolite Identified	**Major metabolites (>10% TRRs)**	Minor metabolites (<10% TRRs)
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C]**	
Peanut hay	Fluoxastrobin (E and Z isomers)	17 other metabolites, no single metabolite was more than 2.7% TRRs, or 3.89 ppm.
Nutmeat	Diastase hydrolysate	4 other metabolites, no single metabolite was more than 4.9% TRRs, or 0.006 ppm.
Metabolite Identified	**Major metabolites (>10% TRRs)**	Minor metabolites (<10% TRRs)
Radiolabel Position	**[Pyrimidine-2-14C]**	
Peanut hay	Fluoxastrobin (E and Z isomers)	16 other metabolites, no single metabolite was more than 2.2% TRRs, or 2.91 ppm.
Nutmeat	Diastase hydrolysate	7 other metabolites, no single metabolite was more than 7.3% TRRs, or 0.011 ppm.

Proposed metabolic scheme in peanut:



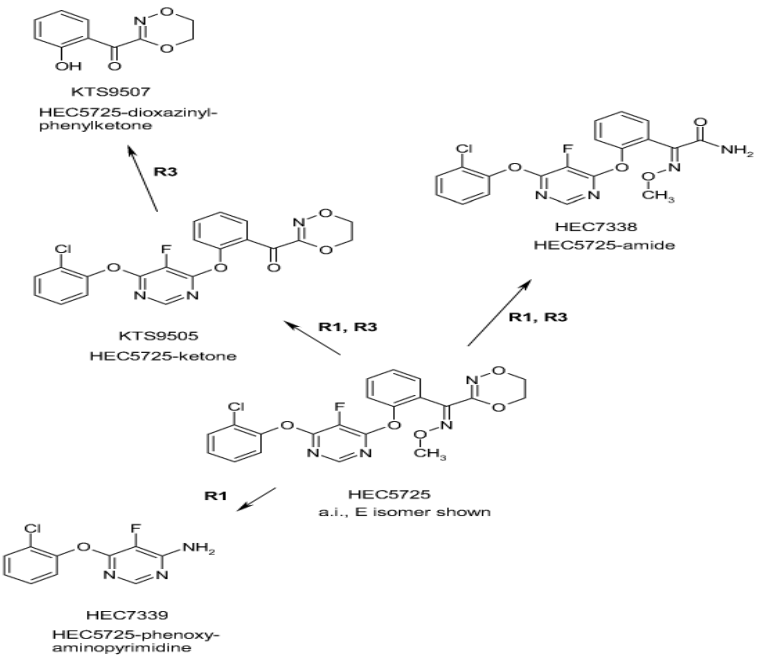
Fluoxastrobin is metabolized in peanuts via the following, or combinations of the following, reactions:

(i) isomerization of the oximether to form the Z isomer of fluoxastrobin;
(ii) oxidative ring opening and degradation of the dioxazine ring;
(iii) cleavage of the oximether, primarily to form HEC5725-ketone;
(iv) nucleophilic substitution of the chlorophenyl ring by glutathione, followed by stepwise degradation of the HEC5725-des-chlorophenyl-glutathione;
(v) cleavage of the parent molecule to form HEC5725-des-pyrimidine and, to a lesser extent, HEC5725-des-chlorophenyl;
(vi) conjugation of hydroxyl and thiol groups to glucosyl and glucosyl-malonyl conjugates; and
(vii) hydroxylation of the chlorophenyl ring (minor reaction).

NATURE OF THE RESIDUE IN PLANTS - Tomato		**PMRA# 1692404 and 1692399**
Radiolabel Position	**[Methoxyiminotolyl-ring-UL-14C] and [Chlorophenyl-UL-14C] Fluoxastrobin**	
Test site	Greenhouse	
Treatment	Foliar spray	
Rate	Three applications for each label. Foliar applications at ~144 g a.i./ha/application	
Timing	1st application: BBCH 64 growth stage. 2nd application: BBCH 72 growth stage. 3rd pplication: BBCH 83 growth stage	
Preharvest interval	Mature tomatoes were harvest 3 days after the last application.	
End-use product	Formulated as a emulsifiable concentrate	
TRRs in Tomato Raw Agriculture Commodities		
Matrix	[Methoxyiminotolyl-ring-UL-14C] (ppm)	[Chlorophenyl-UL-14C] (ppm)
Taomato	0.635	0.418

Metabolite Identified	Major metabolites (>10% TRRs)		Minor metabolites (<10% TRRs)	
Radiolabel Position	**[Methoxyiminotolyl-14C]**	**[Chlorophenyl-14C]**	**[Methoxyiminotolyl-14C]**	**[Chlorophenyl-14C]**
Tomato	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer)	Fluoxastrobin (Z isomer), HEC5725-dioxazinyl-phenylketone, HEC5725-amide, HEC5725-ketone	Fluoxastrobin (Z isomer), HEC5725-phenoxy-aminopyrimidine, HEC5725-amide, HEC5725-ketone

Proposed metabolic scheme in tomato:



R1 = detected with ^{14}C-label ring 1 ([chlorophenyl-UL-^{14}C]HEC5725)
R3 = detected with ^{14}C-label ring 3 ([methoxyiminotolyl-ring-UL-^{14}C]HEC5725), separate report [8]

Fluoxastrobin is metabolized in tomato via hydrolysis or cleavage of the parent molecule to form the dioxazinyl-phenylketone, amide, and ketone metabolites.

CONFINED ACCUMULATION IN ROTATIONAL CROPS – Wheat, Swiss chard and Turnip	**PMRA # 1692482, 1692490, 1692484**
Radiolabel Position	[Methoxyiminotolyl-ring-UL-14C], [Chlorophenyl-UL-14C] and [Pyrimidine-2-14C]
Test site	Greenhouse and outdoor field plots in Germany
Formulation used for trial	Dissolved the reference material in actonitrile/water (1/1, v/v)
Application rate and timing	Fluoxastrobin was applied to soil in planting container at 683 or 840 g a.i./ha. Rotational crops of wheat, Swiss chard and turnip were planted after 30, 150 and 300 days after the application.

TRRs in Raw Agriculture Commodities

Matrix	PBI (days)	[Methoxyiminotolyl-ring-UL-14C]	[Chlorophenyl-UL-14C]	[Pyrimidine-2-14C]
Turnip tops	30	0.020	0.06	0.06
Turnip roots	30	0.012	0.03	0.034
Swiss Chard	30	0.08	0.19	0.156
Wheat Forage	30	0.17	0.10	0.123
Wheat Hay	30	0.50	2.03	0.71
Wheat Straw	30	1.41	2.38	2.44

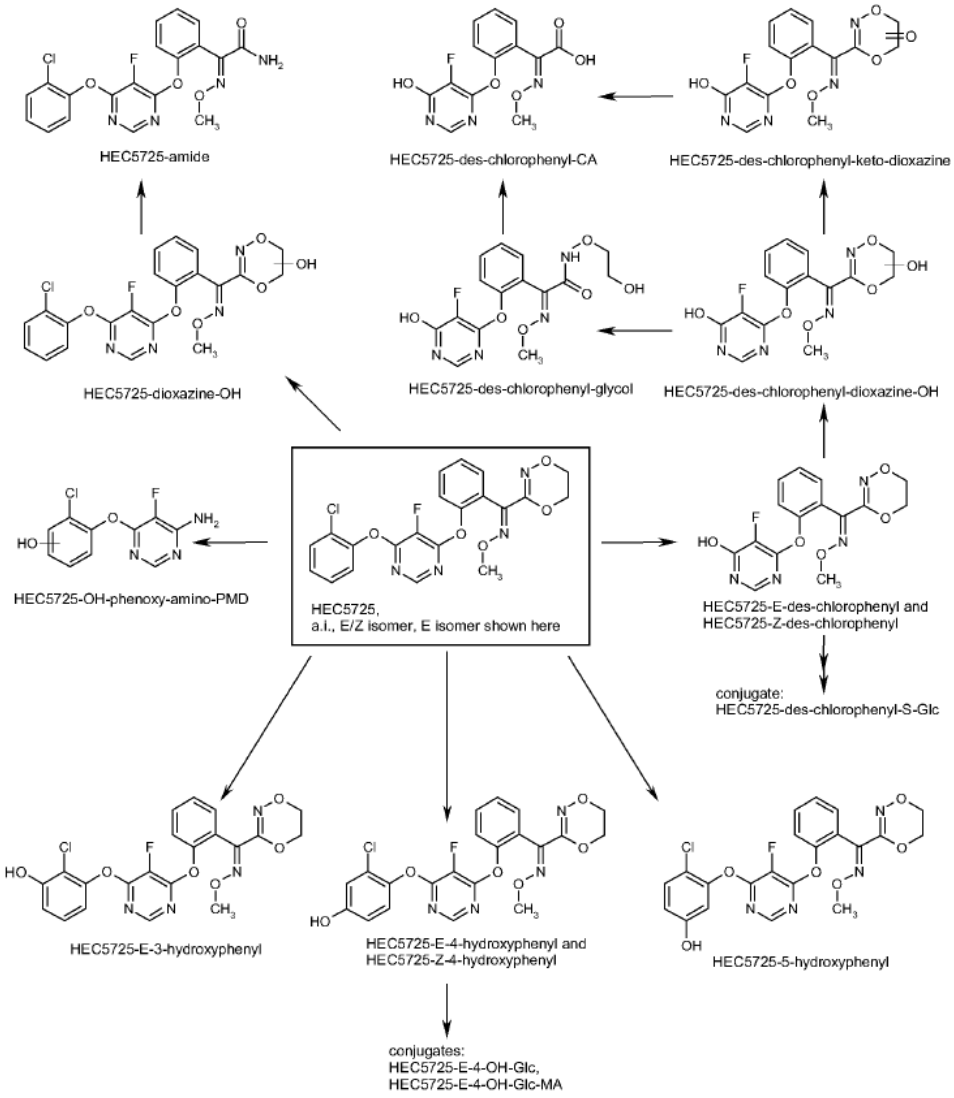
Wheat Grain	30	0.039	0.04	0.107
Turnip tops	157-175	0.028	0.06	0.048
Turnip roots	157-175	0.008	0.03	0.016
Swiss Chard	157-175	0.07	0.15	0.105
Wheat Forage	157-175	0.11	0.11	0.195
Wheat Hay	157-175	0.54	0.31	1.07
Wheat Straw	157-175	1.31	1.10	1.72
Wheat Grain	157-175	0.038	0.03	0.131
Turnip tops	301-328	0.022	0.011	0.055
Turnip roots	301-328	0.006	0.01	0.014
Swiss Chard	301-328	0.06	0.04	0.136
Wheat Forage	301-328	0.23	0.05	0.180
Wheat Hay	301-328	0.37	0.18	0.55
Wheat Straw	301-328	0.56	0.21	0.75
Wheat Grain	301-328	0.032	0.040	0.069
Metabolites Identified		Major Metabolites (> 10% TRR)		
Matrix	PBI (days)	[Methoxyiminotolyl-ring-UL-14C]	[Chlorophenyl-UL-14C]	[Pyrimidine-2-14C]
Wheat Forage	30	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer)
Wheat Hay		Fluoxastrobin (E isomer), and HEC5725-E-4-OH-Glc	Fluoxastrobin (E isomer), HEC5725-E-4-OH-Glc-MA	Fluoxastrobin (E isomer), and HEC5725-E-4-OH-Glc-MA
Wheat Straw		Fluoxastrobin (E isomer), HEC5725-E-4-OH-Glc, and HEC5725-E-4-hydroxyphenyl	Fluoxastrobin (E isomer), HEC5725-E-4-hydroxyphenyl	Fluoxastrobin (E isomer), HEC5725-E-des-chlorophenyl, HEC5725-E-4-hydroxyphenyl
Wheat Grain		None	Fluoxastrobin (E isomer)	None
Turnip tops		Fluoxastrobin (E isomer), HEC5725-E-des-pyrimidine (0.003 ppm)	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer)
Turnip roots		Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer) and HEC5725-E-4-OH-Glc-MA (0.005 ppm)	Fluoxastrobin (E isomer)
Swiss Chard		Fluoxastrobin (E isomer), HEC5725-des-chlorophenyl-dioxazine-OH (0.009 ppm)	Fluoxastrobin (E isomer), and HEC5725-OH-CA-Glc (0.023 ppm)	Fluoxastrobin (E isomer)
Wheat Forage	157-175	Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer), and HEC5725-2-chlorophenol (0.013 ppm)	Fluoxastrobin (E isomer)
Wheat Hay		Fluoxastrobin (E isomer), and HEC5725-E-4-OH-Glc	Fluoxastrobin (E isomer), and HEC5725-2-chlorophenol (0.076 ppm)	Fluoxastrobin (E isomer)
Wheat Straw		Fluoxastrobin (E isomer), and HEC5725-E-4-OH-Glc	Fluoxastrobin (E isomer), HEC5725-2-chlorophenol (0.15 ppm), and HEC5725-E-4-hydroxypenyl (0.14 ppm)	Fluoxastrobin (E isomer) and HEC5725-E-des-chlorophenyl
Wheat Grain		None	Fluoxastrobin (E isomer)	None
Turnip tops		Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer), HEC5725-2-chlorophenol (0.015 ppm)	HEC5725-E-des-chlorophenyl

Turnip roots		n/a	Fluoxastrobin (E isomer), HEC5725-2-chlorophenol (0.003 ppm), and HEC5725-E-4-OH-Glc-MA (0.004 ppm)	HEC5725-E-des-chlorophenyl
Swiss Chard		Fluoxastrobin (E isomer), HEC5725-des-chlorophenyl-dioxazine-OH (0.008 ppm)	Fluoxastrobin (E isomer), HEC5725-2-chlorophenol (0.027 ppm)	HEC5725-E-des-chlorophenyl
Wheat Forage	301-328	Fluoxastrobin (E isomer), HEC5725-des-chlorophenyl-keto-dioxazine, HEC5725-des-chlorophenyl-dioxazine-OH	Fluoxastrobin (E isomer)	HEC5725-E-des-chlorophenyl, HEC5725-des-chlorophenyl-dioxazine-OH, and HEC5725-des-chlorophenyl-keto-dioxazine
Wheat Hay		Fluoxastrobin (E isomer), HEC5725-E-des-chlorophenyl	Fluoxastrobin (E isomer), HEC5725-E-4-OH-Glc (0.016 ppm), and HEC5725-E-4-OH-Glc-MA (0.018 ppm)	HEC5725-E-des-chlorophenyl, and HEC5725-des-chlorophenyl-dioxazine-OH
Wheat Straw		Fluoxastrobin (E isomer)	Fluoxastrobin (E isomer), HEC5725-2-chlorophenyl (0.023 ppm), and HEC5725-E-4-OH-Glc (0.029 ppm), and HEC5725-E-4-hydrocyphenyl (0.021 ppm)	HEC5725-E-des-chlorophenyl, and HEC5725-des-chlorophenyl-dioxazine-OH
Wheat Grain		None	Fluoxastrobin (E isomer)	None
Turnip tops		FLuoxastrobin (E isomer)	None	HEC5725-E-des-chlorophenyl (0.007 ppm)
Turnip roots		n/a	n/a	n/a
Swiss Chard		HEC5725-E-des-chlorophenyl (0.007 ppm)	Fluoxastrobin (E isomer) and HEC5725-OH-CA-Glc (0.006 ppm)	HEC5725-E-des-chlorophenyl (0.030 ppm) and HEC5725-des-chlorophenyl-keto-dioxazine (0.017 ppm)
Metabolites Identified		Minor Metabolites (>10% TRR)		
Matrix	PBI (days)	[Methoxyiminotolyl-ring-UL-14C]	[Chlorophenyl-UL-14C]	[Pyrimidine-2-14C]
Wheat Forage	30	Fluoxastrobin (Z isomer), and 11 metabolites with no single metabolite was more than 8.6% TRRs (or 0.015 ppm)	Fluoxastrobin (Z isomer) and 13 metabolites with no single metabolite was more than 9.3% TRRs (or 0.009 ppm)	Fluoxastrobin (Z isomer) and 8 metabolites with no single metabolite was more than 7.9% TRRs (or 0.10 ppm)
Wheat Hay		7 metabolites with no single metabolite was more than 4.6% TRRs (or 0.02 ppm)	Fluoxastrobin (Z isomer) and 12 metabolites with no single metabolite was more than 4.4% TRRs (or 0.09 ppm)	Fluoxastrobin (Z isomer) and 11 metabolites with no single metabolite was more than 7.5% TRRs (or 0.05 ppm)

Wheat Straw		Fluoxastrobin (Z isomer), and 9 metabolites with no single metabolite was more than 7.2% TRRs (or 0.099 ppm)	Fluoxastrobin (Z isomer) and 14 metabolites with no single metabolite was more than 6.1% TRRs (or 0.14 ppm)	Fluoxastrobin (Z isomer) and 13 metabolites with no single metabolite was more than 5.4% TRRs (or 0.13 ppm)
Wheat Grain		5 metabolites with no single metabolite was more than 9.8% TRRs (or 0.004 ppm)	Fluoxastrobin (Z isomer) and 14 metabolites with no single metabolite was more than 3.2% TRRs (or 0.001 ppm)	Fluoxastrobin (E and Z isomer) and 3 metabolites with no single metabolite was more than 7.7% TRRs (or 0.008 ppm)
Turnip tops		Only two metabolites were observed with <5.3% TRRs (or <0.001 ppm)	Fluoxastrobin (Z isomer) and 14 metabolites with no single metabolite was more than 5.1% TRRs (or 0.010 ppm)	Fluoxastrobin (Z isomer) and 6 metabolites with no single metabolite was more than 5.4% TRRs (or 0.003 ppm)
Turnip roots		Only two metabolites were observed with <6.5% TRRs (or <0.001 ppm)	Fluoxastrobin (Z isomer) and 6 metabolites with no single metabolite was more than 5.8% TRRs (or 0.002 ppm)	Fluoxastrobin (Z isomer) and 6 metabolites with no single metabolite was more than 9.0% TRRs (or 0.14 ppm)
Swiss Chard		7 metabolites with no single metabolite was more than 6.7% TRRs (or 0.005 ppm)	Fluoxastrobin (Z isomer) and 4 metabolites with no single metabolite was more than 3.0% TRRs (or 0.002 ppm)	Fluoxastrobin (Z isomer) and 4 metabolites with no single metabolite was more than 8.8% TRRs (or 0.003 ppm)
Wheat Forage	157-175	Fluoxastrobin (Z isomer), and 10 metabolites with no single metabolite was more than 4.9% TRRs (or 0.005 ppm)	4 metabolites with no single metabolite was more than 4.6% TRRs (or 0.005 ppm)	6 metabolites with no single metabolite was more than 7.8% TRRs (or 0.015 ppm)
Wheat Hay		Fluoxastrobin (Z isomer), and 11 metabolites with no single metabolite was more than 7.4% TRRs (or 0.04 ppm)	Fluoxastrobin (Z isomer) and 5 metabolites with no single metabolite was more than 7.7% TRRs (or 0.024 ppm)	Fluoxastrobin (Z isomer) and 13 metabolites with no single metabolite was more than 9.0% TRRs (or 0.010 ppm)
Wheat Straw		Fluoxastrobin (Z isomer), and 14 metabolites with no single metabolite was more than 5.9% TRRs (or 0.08 ppm)	Fluoxastrobin (Z isomer) and 4 metabolites with no single metabolite was more than 7.7% TRRs (or 0.08ppm)	Fluoxastrobin (Z isomer) and 12 metabolites with no single metabolite was more than 8.0% TRRs (or 0.014 ppm)
Wheat Grain		3 metabolites with no single metabolite was more than 8.1% TRRs (or 0.003 ppm)	Fluoxastrobin (Z isomer) and 8 metabolites with no single metabolite was more than 2.1% TRRs (or <0.001 ppm)	Fluoxastrobin (E isomer) and 3 metabolites with no single metabolite was more than 5.6% TRRs (or 0.007 ppm)
Turnip tops		5 metabolites with no single metabolite was more than 8.5% TRRs (or 0.002 ppm)	5 metabolites with no single metabolite was more than 3.5% TRRs (or 0.002 ppm)	Fluxastrobin (E isomer) and 6 metabolites with no single metabolite was more than 5.0% TRRs (or 0.002 ppm)
Turnip roots		n/a	2 metabolites with no single metabolite was more	HEC5725-OH-phenoxy-amino-PMD

			than 5.0% TRRs (or 0.002 ppm)	
Swiss Chard		Fluoxastrobin (Z isomer), and 5 metabolites with no single metabolite was more than 6.1% TRRs (or 0.004 ppm)	6 metabolites with no single metabolite was more than 8.6% TRRs (or 0.002 ppm)	4 metabolites with no single metabolite was more than 9.5% TRRs (or 0.010 ppm)
Wheat Forage	301-328	5 metabolites with no single metabolite was more than 8.6% TRRs (or 0.020 ppm)	Fluoxastrobin (Z isomer) and 5 metabolites with no single metabolite was more than 4.0% TRRs (or 0.002 ppm)	Fluoxastrobin (E isomer) and 5 metabolites with no single metabolite was more than 2.0% TRRs (or 0.004 ppm)
Wheat Hay		8 metabolites with no single metabolite was more than 6.8% TRRs (or 0.02 ppm)	Fluoxastrobin (Z isomer) and 4 metabolites with no single metabolite was more than 3.5% TRRs (or 0.006 ppm)	Fluoxastrobin (E and Z isomers) and 5 metabolites with no single metabolite was more than 7.7% TRRs (or 0.042 ppm)
Wheat Straw		12 metabolites with no single metabolite was more than 8.6% TRRs (or 0.05 ppm)	Fluoxastrobin (Z isomer) and 4 metabolites with no single metabolite was more than 5.5% TRRs (or 0.012 ppm)	Fluoxastrobin (E and Z isomers) and 13 metabolites with no single metabolite was more than 6.4% TRRs (or 0.048 ppm)
Wheat Grain		3 metabolites with no single metabolite was more than 6.9% TRRs (or 0.002 ppm)	None	4 metabolites with no single metabolite was more than 5.6% TRRs (or 0.004 ppm)
Turnip tops		5 metabolites with no single metabolite was more than 8.6% TRRs (or 0.005 ppm)	4 metabolites with no single metabolite was more than 6.9% TRRs (or 0.001 ppm)	Fluoxastrobin (E isomer) and 4 metabolites with no single metabolite was more than 4.5% TRRs (or 0.002 ppm)
Turnip roots		n/a	n/a	n/a
Swiss Chard		Fluoxastrobin (E isomer), and 4 metabolites with no single metabolite was more than 9.5% TRRs (or 0.002 ppm)	2 metabolites with no single metabolite was more than 8.8% TRRs (or 0.004 ppm)	Fluoxastrobin (E isomer) and 4 metabolites with no single metabolite was more than 9.1% TRRs (or 0.012 ppm)

Proposed metabolic scheme in rotational plants:



The major metabolic route of fluoxastrobin in rotated crop matrices was hydroxylation, especially at the 4-position of the chlorophenyl moiety to yield HEC5725-E-4-hydroxyphenyl; glucose and glucose malonic acid conjugates of this metabolite were also observed. A second important metabolic route was cleavage of fluoxastrobin to yield HEC5725-E-des-chlorophenyl, which was further metabolized by hydroxylation to HEC5725-deschlorophenyl-dioxazine-OH. HEC5725-des-chlorophenyl-dioxazine-OH was partly cleaved to form HEC5725-des-chlorophenyl-glycol, which was oxidized to HEC5725-des-chlorophenyl-CA. HEC5725-des-chlorophenyl-dioxazine-OH was also oxidized to HEC5725-deschlorophenyl-keto-dioxazine, which cleaved to form HEC5725-des-chlorophenyl-CA. Cleavage of the ether bridge between the pyrimidine and methoxyiminotolyl rings of the parent compound was a minor metabolic route in rotational crops, yielding HEC5725-E-des pyrimidine. Another minor metabolic route was hydroxylation of the parent compound in the dioxazine ring, followed by oxidative cleavage and hydrolysis to form HEC5725-amide.

Field Accumulation in Rotational Crops – Mustard green, Turnip and Wheat	**PMRA# 1737143**

A limited field rotational crop study on the representative crops mustard greens (leafy vegetable), turnips (root vegetable), and wheat (cereal grain). Three trial sites, in Regions 2 (GA), 3 (FL), and 10 (CA), were used for each crop. At each trial site, four spray applications of the suspension concentrate formulation (SC, 400 g a.i./L) were made to bare soil at ~202 g a.i./ha/application, for a total rate of ~808 g a.i./ha. Rotational crops were planted at ~1, 4, 8, and 12 months after the last application and grown to maturity; separate plots with different application timings were used for each crop at each plantback interval (PBI).

At the 1-month PBI, combined residues of fluoxastrobin (E and Z isomers) were below the method LOQ (<0.01 ppm) in mustard greens and turnip tops and roots, <0.01-0.0658 ppm in wheat grain, 0.0117-0.1140 ppm in wheat forage, 0.0305-0.1210 ppm in wheat hay, and 0.0117-0.0551 ppm in wheat straw. At the 4-month PBI, combined residues of fluoxastrobin were <0.01 ppm in wheat grain, <0.01-0.0829 ppm in wheat forage, <0.01-0.0522 ppm in wheat hay, and <0.01-0.0218 ppm in wheat straw. At the 8-month PBI, combined residues of fluoxastrobin were <0.01 ppm in wheat grain, <0.01-0.0120 ppm in wheat forage, <0.01-0.0105 ppm in wheat hay, and <0.01-0.0105 ppm in wheat straw.

Because residues of fluoxastrobin (E and Z isomers) were below the method LOQ (<0.01 ppm) in all samples of rotated mustard greens and turnip tops and roots from the 1-month PBI, samples of these commodities from the 4-, 8-, and 12-month PBIs were not analyzed. Similarly, because residues of fluoxastrobin (E and Z isomers) were at or below the method LOQ (≤0.01 ppm) in all samples of rotated wheat commodities from the 8-month PBI, samples of rotated wheat commodities from the 12-month PBI were not analyzed.

Commodity	Total Rate (g a.i./ha)	PBI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Mustard greens	806-818	30-32	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Turnip tops			3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Turnip roots			3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Wheat forage	795-806	29-32	3	0.012	0.114	0.114	0.018	0.050	0.06
	806-829	119-122	3	<0.01	0.082	0.082	0.013	0.035	0.04
	806-818	230-241	3	<0.01	0.011	0.011	0.010	0.010	0.0007
Wheat hay	795-806	29-32	3	0.031	0.108	0.108	0.032	0.057	0.04
	806-829	119-122	3	<0.01	0.043	0.043	0.020	0.024	0.02
	806-818	230-241	3	<0.01	0.010	0.010	0.010	0.010	0.0001
Wheat grain	795-806	29-32	3	<0.01	0.0647	0.0647	0.01	0.028	0.03
	806-829	119-122	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
	806-818	230-241	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Wheat straw	795-806	29-32	3	0.020	0.053	0.053	0.020	0.031	0.02
	806-829	119-122	3	<0.01	0.020	0.020	0.018	0.016	0.005
	806-818	230-241	3	<0.01	<0.01	<0.01	<0.01	<0.01	0

Field Accumulation in Rotational Crops – Legume Vegetable **PMRA# 1737137**

A field rotational crop study on legume vegetables (succulent edible-podded beans, succulent shelled beans, dried shelled beans, succulent edible-podded peas, succulent shelled peas, dried shelled peas, and soybeans; Crop Group 6) and foliage of legume vegetable (forage and hay of cowpea, field pea, and soybean; Crop Group 7). A total of 56 trials were conducted on rotated legume vegetables during the 2000-2001 growing season. Six trials were conducted on succulent edible-podded beans in Regions 1 (PA; 1 trial), 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (IN and NE; 2 trials), and 11 (WA; 1 trial). Six trials were conducted on succulent shelled beans in Regions 2 (GA and NJ; 3 trials), 5 (WI; 1 trial), 10 (CA; 1 trial), and 11 (OR; 1 trial). Twelve trials were conducted on dried shelled beans (including cowpeas) in Regions 2 (GA, 1 trial), 4 (MS, 1 trial), 5 (IN, KS, ND, and NE, 1 trial each), 6 (TX, 1 trial), 7 (ND, 1 trial), 8 (TX, 1 trial), 9 (UT, 1 trial), 10 (CA, 1 trial), and 11 (OR, 1 trial). Three trials were conducted on succulent edible-podded peas in Regions 5 (WI, 1 trial), 11 (WA, 1 trial), and 12 (OR, 1 trial). Six trials were conducted on succulent shelled peas in Regions 2 (NJ, 1 trial), 5 (MN and WI, 3 trials), 11 (ID, 1 trial), and 12 (OR, 1 trial). Eight trials were conducted on dried shelled peas (including field peas) in Region 11 (ID, OR, and WA). Fifteen trials were conducted on soybeans in Regions 2 (GA; 2 trials), 4 (AR and MS; 2 trials), and 5 (IA, IL, IN, KS, MO, NE, and OH; 11 trials).

The residues of fluoxastrobin (sum of E and Z isomers) were 0.641-3.26 ppm in/on untrimmed celery and 0.017-0.465 ppm in/on trimmed celery harvested 3-4 days following the four broadcast foliar applications of fluoxastrobin at total seasonal rates of 795-952 g a.i./ha. It was noted that trimming the celery leaf stalk yields an average residue reduction of 14 times.

Combined residues of fluoxastrobin (sum of E and Z isomers) were below the LOQ (<0.01 ppm) in rotated succulent edible-podded beans, succulent shelled beans, dried shelled beans, succulent edible-podded peas, succulent shelled peas, dried shelled peas, and soybean seed planted 26-33 days following treatment to bare soil. Combined residues of fluoxastrobin were <0.01 ppm in rotated cowpea hay, field pea forage, and field pea hay, <0.01-0.03 ppm in rotated

cowpea forage, <0.01-0.046 ppm in rotated soybean forage, and <0.01-0.029 ppm in rotated soybean hay planted 28-33 days following treatment to bare soil.

Commodity	Total Rate (g a.i./ha)	PBI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Succulent edible-podded beans	806-829	28-32	6	<0.01	<0.01	<0.01	<0.01	<0.01	0
Succulent shelled beans	806-818	28-30	6	<0.01	<0.01	<0.01	<0.01	<0.01	0
Dried shelled beans	806-818	28-31	9	<0.01	<0.01	<0.01	<0.01	<0.01	0
Succulent edible-podded peas	806-840	28	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Succulent shelled peas	806-829	26-30	6	<0.01	<0.01	<0.01	<0.01	<0.01	0
Dried shelled peas	784-818	27-31	5	<0.01	<0.01	<0.01	<0.01	<0.01	0
Cowpea forage	795-806	29-30	3	<0.01	0.026	0.026	0.01	0.015	0.009
Cowpea hay	795-806	29-30	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Field pea forage	806-818	28-31	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Field pea hay	806-818	28-31	3	<0.01	<0.01	<0.01	<0.01	<0.01	0
Soybean seed	795-806	28-33	15	<0.01	<0.01	<0.01	<0.01	<0.01	0
Soybean forage	795-806	28-33	15	<0.01	0.0447	0.0447	0.01	0.0127	0.009
Soybean hay	795-806	28-33	15	<0.01	0.0257	0.0257	0.0103	0.0143	0.006

Field Accumulation in Rotational Crops – Alfalfa **PMRA# 1737140**

A field rotational crop study on alfalfa. Twelve alfalfa trials were conducted in Regions 1 (PA; 1 trial), 2 (VA; 1 trial), 5 (IN, KS, MI, ND, NE, OR; 6 trials), 7 (ND; 1 trial), 9 (UT; 1 trial), 10 (CA; 1 trial), and 11 (WA; 1 trial).

Combined residues of fluoxastrobin (sum of E and Z isomers) were <0.01-0.034 ppm in alfalfa forage and <0.01-0.055 ppm in alfalfa hay planted 26-32 days following treatment to the bare soil. Second and third cuttings of alfalfa were not collected because of the early plantback interval.

Commodity	Total Rate (g a.i./ha)	PBI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Alfalfa forage	795-829	26-32	12	<0.01	0.0325	0..0325	0.01	0.0122	0.006
Alfalfa hay		26-32	12	<0.01	0.053	0.053	0.01	0.0162	0.015

Field Accumulation in Rotational Crops – Grasses **PMRA# 1737141**

A field rotational crop study on grasses. Twelve grass trials (4 trials each of bluegrass, bermudagrass, and fescue) were conducted in Regions 1 (PA; 1 trial), 2 (GA; 1 trial), 3 (FL; 1 trial), 4 (MS; 1 trial), 5 (IN and KS; 2 trials), 9 (UT; 1 trial), 10 (AZ; 1 trial), 11 (ID and WA; 2 trials), and 12 (OR; 2 trials).

Combined residues of fluoxastrobin (sum of E and Z isomers) were <0.01-0.066 ppm in grass forage and <0.01-0.328 ppm in grass hay planted 26-31 days following treatment to the bare soil.

Commodity	Total Rate (g a.i./ha)	PBI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Grass forage	795-851	26-31	12	<0.01	0.063	0.063	0.015	0.018	0.015
Grass hay		26-31	12	<0.01	0.322	0.322	0.016	0.048	0.088

Field Accumulation in Rotational Crops – Corn, Rice, Sorghum and Wheat | **PMRA# 1737144**

A field rotational crop study on cereal grains (corn, rice, sorghum, and wheat; Crop Group 15) and the forage, fodder, and straw of cereal grains (Crop Group 16). A total of 55 trials were conducted during the 2000-2001 growing season. Nineteen trials were conducted on corn: fifteen trials were conducted on field corn (forage, grain, and stover) in Regions 1 (NY; 1 trial), 2 (GA; 1 trial), 5 (IA, IL, IN, KS, and NE; 12 trials), and 6 (OK; 1 trial); four trials were conducted on sweet corn [forage, kernel plus cob with husk removed (K+CWHR), and stover] in Regions 3 (FL; 1 trial), 10 (CA; 1 trial), 11 (OR; 1 trial), and 12 (OR; 1 trial). In addition, at five of the field corn trials, in Regions 1 (NY; 1 trial), 2 (GA; 1 trial), and 5 (IN, KS, and NE; 3 trials), samples of field corn K+CWHR were collected. Twelve trials were conducted on rice (grain and straw) in Regions 4 (LA and MS; 7 trials), 5 (MO; 1 trial), 6 (TX; 2 trials), and 10 (CA; 2 trials). Nine trials were conducted on sorghum (forage, grain, and straw) in Regions 4 (MS; 1 trial), 5 (IN, KS, and NE; 3 trials), 6 (OK; 2 trials), 7 (SD; 1 trial), and 8 (OK and TX; 2 trials). Fifteen trials were conducted on wheat (forage, hay, grain, and straw) in Regions 2 (GA; 1 trial), 4 (MS; 1 trial), 5 (KS, ND, and NE; 3 trials), 6 (OK; 1 trial), 7 (ND and SD; 4 trials), 8 (OK and TX; 4 trials), and 11 (OR; 1 trial).

Fluoxastrobin (sum of E and Z isomers) residues were each below the LOQ (<0.01 ppm) in all samples of rotated field corn grain, rice grain, sorghum grain, and wheat grain and were below the LOQ in 17 of 18 samples of rotated corn K+CWHR planted 27-39 days following treatment to bare soil. One sample of sweet corn K +CWHR bore quantifiable residues of fluoxastrobin (sum of E and Z isomers) at 0.016 ppm. Combined residues of fluoxastrobin were <0.01-0.038 ppm in rotated corn forage, <0.01-0.094 ppm in rotated corn stover, <0.01 ppm in rotated rice straw, <0.01 ppm in rotated sorghum forage, <0.01-0.013 ppm in rotated sorghum stover, <0.01-0.084 ppm in rotated wheat forage, <0.01-0.078 ppm in rotated wheat hay, and <0.01-0.063 ppm in rotated wheat straw planted 27-39 days following treatment to bare soil.

Commodity	Total Rate (g a.i./ha)	PBI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Corn Forage	795-829	27-31	19	<0.01	0.036	0.036	0.01	0.012	0.006
Corn Stover	795-829	27-31	19	<0.01	0.093	0.093	0.01	0.017	0.019
Field Corn Grain	795-806	27-31	15	<0.01	<0.01	<0.01	<0.01	<0.01	0
K+CWHR	795-829	27-31	9	<0.01	0.013	0.013	0.01	0.010	0.001
Rice Grain	795-840	27-37	12	<0.01	<0.01	<0.01	<0.01	<0.01	0
Rice Straw	795-840	37-37	12	<0.01	<0.01	<0.01	<0.01	<0.01	0
Sorghum Forage	795-818	28-39	9	<0.01	<0.01	<0.01	<0.01	<0.01	0
Sorghum grain	795-818	28-39	9	<0.01	<0.01	<0.01	<0.01	<0.01	0
Sorghum Stover	795-818	28-39	9	<0.01	0.011	0.011	0.01	0.010	0.0003
Wheat Forage	604-818	27-34	15	<0.01	0.083	0.083	0.01	0.0186	0.019
Wheat Hay	604-818	27-34	15	<0.01	0.0685	0.0685	0.018	0.024	0.017
Wheat Grain	604-818	27-34	15	<0.01	<0.01	<0.01	<0.01	<0.01	0
Wheat Straw	604-818	27-34	15	<0.01	0.0605	0.0605	0.0195	0.025	0.017

CROP FIELD TRIALS and Residue Decline on Celery | **PMRA# 1737120**

A total of 8 celery field trials were conducted in Regions 3 (FL; 2 trials), 5 (OH; 1 trial), and 10 (CA; 5 trials) in the US during the 2000 and 2001 growing seasons. At each test location, a total of four broadcast foliar spray applications of the suspension concentrate formulation were made at ~202 g a.i./ha/application with a 5 to 9 day retreatment interval, for total seasonal rates of ~806 g a.i./ha. Applications were made in ~202-404 L/ha of water using ground equipment (one application at one trial was made in 1348 L/ha); no adjuvant was added to the spray mixtures. Samples of untrimmed and trimmed celery were harvested from all test sites 3-4 days following the last application. Additional samples were collected from one trial 0, 7, and 14 days following the last application to evaluate the residue decline.

The residues of fluoxastrobin (sum of E and Z isomers) were 0.641-3.26 ppm in/on untrimmed celery and 0.017-0.465 ppm in/on trimmed celery harvested 3-4 days following the four broadcast foliar applications of fluoxastrobin at total seasonal rates of 795-952 g a.i./ha. It was noted that trimming the celery leaf stalk yields an average residue reduction of 14 times.

Residue decline data show that residues of fluoxastrobin (sum of E and Z isomers) decreased in celery with increasing pre-harvest intervals (PHIs). Average residues in untrimmed celery collected from a single field trial were 2.40 ppm in samples from the 0-day PHI and decreased to 0.77 ppm by the 14-day PHI.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Celery, untrimmed	795-952	3-4	8	0.790	3.10	3.10	2.21	2.09	0.78
Celery, trimmed		3-4	7	0.018	0.407	0.407	0.212	0.201	0.15

CROP FIELD TRIALS and Residue Decline on Field Corn **PMRA# 1737124**

A total of twenty one field trials were conducted in the United States in Regions 1 (OH), 2 (GA, 2 trials), 5 (IN, KS, MI, SD, 1 trial each; MN, IL, OH, 2 trials each; IA, 3 trials; NE, 4 trials), and 6 (TX) during the 2007 growing season. At each test location, the treated plots received two foliar applications of a suspension concentrate (SC) formulation of fluoxastrobin containing 40.3% of the active ingredient at 202 g a.i./ha/application, with one exception (trial 11 at 165/202 g a.i./ha/application) using a spray volume of approximately 225 L/ha. In addition, at one site, the Evito 480 SC Fungicide was applied in a total spray volume of 1125 L/ha to simulate an aerial application. No adjuvant was used in all applications. Applications were made beginning when disease first developed or just before tassle emergence (BBCH 51-65) and again at 30 days before harvest (BBCH 85-87) using ground-based equipment, at retreatment intervals (RTI) of 32-71 days. Samples of grain and fodder were harvested at PHIs of 30-52 days and forage at 0-day. In two trials, decline samples of forage were collected at 0, 10, 20, and 27 (only one trial) days after last application (DALA). Zero-time samples were collected at a minimum of one hour after application and after the spray had dried.

The results from these trials show that fluoxastrobin residues (sum of E and Z isomers) ranged from < LOQ-2.67 ppm in corn forage, 0.39-4.24 ppm in corn fodder, and below the quantitation limit (<0.02 ppm) in corn grain samples. Residue decline data show that fluoxastrobin decreases in corn forage with increasing PHIs from 0 to 27 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Forage	403	0	21	0.37	2.0	2.0	1.5	1.5	0.36
Fodder		30-52	21	0.47	3.7	3.7	0.76	1.2	0.97
Grain		30-52	21	<0.02	<0.02	<0.02	<0.02	<0.02	0

CROP FIELD TRIALS and Residue Decline on Sweet Corn **PMRA# 1737126**

Ten sweet corn field trials were conducted in the U.S. during the 2008 growing season in Regions 1 (VA; 1 trial), 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (MI and MN; 3 trials), 7 (ND; 1 trial), 10 (CA; 1 trial), 11 (ID; 1 trial), and 12 (OR; 1 trial). At each treated plot, a 400 g a.i./L SC formulation of fluoxastrobin was applied to sweet corn as four broadcast foliar applications at 135-146 g a.i./ha/application for a total application rate of 537-583 g a.i./ha. Retreatment intervals (RTIs) were 13-16 days, except at one trial where the final application was made at a 21-day RTI. The petitioner stated that the use pattern was targeted to allow for 14-day retreatment intervals and a 7-day PHI for forage and kernels plus cobs with husks removed (K +CWHR). Applications were made using ground equipment in spray volumes of 147 L/ha and an adjuvant was added to the spray mixture for some applications at 0.05-0.25% (v/v). Single control and duplicate treated samples of sweet corn forage and K +CWHR were harvested from each site 7-8 days after final application, except at one field trial where samples were harvested within 3 days due to a bacterial infection which threatened to degrade the crop. Samples of sweet corn stover were harvested from each site 23-35 days after the final application. At two sites, additional samples of sweet corn forage and K +CWHR were harvested 2-3, 10, and 14-15 days after final application to assess residue decline.

Following four foliar broadcast applications of the SC formulation at 537-583 g a.i./ha, residues of fluoxastrobin were 0.34-5.15 ppm in/on forage and 0.25-5.68 ppm in/on stover. Quantifiable combined residues at 0.01 ppm (LOQ) were observed in/on one sample of K+CWHR; residues in remaining samples were <LOQ. In the residue decline studies, the average fluoxastrobin residues declined or increased slightly in forage with increasing PHIs from 2-15 days. Fluoxastrobin residues were all below LOQ in K+CWHR samples from the decline trials with PHIs of 2-15 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Forage	537-583	7-8	10	0.465	4.78	4.78	2.37	2.33	1.60
Stover		23-35	10	0.305	4.71	4.71	1.19	1.64	1.42
K+CWHR		7-8	10	<0.01	<0.01	<0.01	<0.01	<0.01	0

CROP FIELD TRIALS and Residue Decline on Wheat **PMRA# 1737130**

Twenty-five wheat field trials were conducted in the U.S. and Canada. Seventeen field trials were conducted in the U.S. during the 2007-2008 growing seasons in Regions 2 (GA; 1 trial), 4 (AR; 1 trial), 5 (MI and NE; 3 trials), 6 (OK; 1 trial), 7 (ND and SD; 6 trials), 8 (KS, OK, and TX; 4 trials), and 11 (ID; 1 trial), and eight trials were conducted in Canada during the 2008 growing season in Region 14 (AB, MB, and SK). At each treated plot, a 400 g a.i./L SC formulation of fluoxastrobin was applied to wheat as two broadcast foliar applications at 134-146 g a.i./ha/application for a total application rate of 268-292 g a.i./ha/season. The first applications were made to wheat plants at BBCH 30-69 growth stages, and the second applications were made at BBCH 51-75 growth stages; RTIs were 7-26 days. The petitioner stated that the target growth stages were at BBCH 29-37 and 59 for first and second applications, respectively. Applications were made using ground equipment in spray volumes of 146-235 L/ha. A non-ionic surfactant (NIS) was added to the spray mixtures in two U.S. trials and six Canadian trials at 0.125% or 0.2% (v/v).

Combined residues of fluoxastrobin (E and Z isomers) were 0.27-4.14 ppm in/on forage following a single broadcast foliar application of the SC formulation at 134-146 g a.i./ha, and were 0.69-10.57 ppm in/on hay, <0.01-0.11 ppm in/on grain, and 0.18-14.55 ppm in/on straw following two applications for a total rate of 268-292 g a.i./ha.

In the eight trials reflecting use of a spray adjuvant, use of an NIS appeared to result in higher residues in/on forage, and slightly higher residues in/on hay. Combined residues of fluoxastrobin (E and Z isomers) in samples from the eight trials including NIS adjuvants were 0.68-4.14 ppm in/on forage (excluding results for the decline trial in Canada), and 2.34-9.43 ppm in/on hay. In trials in which a surfactant was not used, residues were 0.27-3.74 ppm in/on forage, and 0.69-10.57 ppm in/on hay. Use of surfactants did not appear to affect residues in grain and straw; residues were <0.01-0.01 ppm in/on all grain samples from these trials and 0.18-0.41 ppm in/on all straw samples.

In the residue decline trials, combined residues of fluoxastrobin generally declined in forage with increasing sampling interval from 0 to 14 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Wheat forage	134-146	6-13	23	0.28	4.0	4.0	1.1	1.7	1.2
Wheat hay	268-292	6-11	25	0.77	9.9	9.9	4.4	4.9	2.7
Wheat straw		21-69	25	0.20	12.3	12.3	0.75	1.8	2.9
Wheat grain		21-69	25	<0.01	0.11	0.11	0.01	0.02	0.03

CROP FIELD TRIALS and Residue Decline on Barley **PMRA# 1737134**

Twelve field trials (1 trial each in Regions 5 and 7, 10 trials in Region 14) in the US and Canada were conducted to evaluate the quantity of fluoxastrobin residues in barley hay, grain and straw following two foliar applications of Evito 480 SC Fungicide, a suspension concentrate formulation containing 480 g a.i./L. The nominal application rate was 140 g a.i./ha/application. The first application at each trial was targeted to occur when the barley crop was at the Feekes 5-8 growth stage. The second application at each trial was targeted to occur when the barley crop was at 10.3 to 10.5 growth stages. Adjuvant was added to the spray mixture for applications.

Hay samples were harvested at 7 days after the second application and field-dried to a moisture content of approximately 20%. Barley grain was collected at maturity and separated from the dried stems, stalk, and leaves. Barley straw was collected after it was allowed to dry naturally as a result of the senescence of the plant after the grain matured. Additional samples were collected at two trial sites to establish a residue decline profile. Barley hay was targeted for collection at 0, 3, 7, 10, and 14 days after the second application. Barley grain and straw were targeted for collection starting when approximately half of the grain reached Feekes 11.2 then 7, 10, 14, and 21 days after the initial sample collection.

The maximum fluoxastrobin (sum for E and Z isomers) residues were reported as 11.45 ppm in hay at PHIs of 6 to 8 days, 0.09 ppm in grain at PHIs of 26 to 58 days and 1.81 ppm in straw at PHIs of 26 to 58 days. Residue values clearly declined during the five hay samplings with increasing PHIs from 0 to 14 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Barley Hay	268-276	6-8	12	1.42	11.45	11.45	5.45	5.72	2.3
Barley Straw		37-58	12	0.45	1.92	1.92	1.03	1.01	0.13
Barley Grain			12	<0.01	0.091	0.091	0.026	0.037	0.03

CROP FIELD TRIALS and Residue Decline on Soybean **PMRA# 1737125**

A total of twenty field trials were conducted in the US in Regions 2 (GA, 2 trials), 4 (AR, MS, LA, 1 trial each), and 5 (IN, MO, KS, OH, MN, 1 trial each; IA, IL, MI, SD, NE, 2 trials each) during the 2007 growing season. At each test location, the treated plots received two foliar applications of a SC formulation of fluoxastrobin containing 40.3% of the active ingredient at 202 g a.i./ha/application using a spray volume of approximately 225 litres/ha. In addition, at one site the Evito 480 SC Fungicide was applied in a total spray volume of 1125 litres/ha to simulate an aerial application. No adjuvant was used in the applications. Applications were made at approximately BBCH 69-70 and again at approximately BBCH 77-79 stages of growth using ground-based equipment. Samples of soybean seed and hay were harvested at normal harvest at PHIs of 25-53 days. Soybean forage was collected at 0-3 DALA. In two trials, decline samples of forage were collected at 0, 5, 12-15, and 20-23 DALA.

The results from these trials show that fluoxastrobin residues (sum of E and Z isomers) ranged from < 0.02 ppm (LOQ)-0.038 ppm in seed, 0.084-1.19 ppm in hay, and 1.30-9.39 ppm in forage. Residue decline data show that fluoxastrobin decreases in soybean forage with increasing PHIs from 0 to 23 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Soybean forage	403	0-3	20	2.07	9.09	9.09	3.41	3.94	1.67
Soybean hay		25-53	20	0.092	0.870	0.870	0.485	0.462	0.22
Soybean seed		25-53	20	<0.02	0.031	0.031	0.02	0.021	0.003

CROP FIELD TRIALS and Residue Decline on Potato **PMRA# 1737121**

A total of 27 potato field trials were conducted in the US and Canada during the 2000 and 2001 growing seasons. Seventeen trials were conducted in the US in Regions 1 (NY and PA; 2 trials), 2 (NC; 1 trial), 3 (FL; 1 trial), 5 (IN, MN, and ND; 4 trials), 5A (MI; 1 trial), 9 (UT; 1 trial), 10 (CA; 1 trial), and 11 (ID, OR, and WA; 6 trials). Ten trials were conducted in Canada in Regions 1 (NB; 1 trial), 1A (NS; 4 trials), 5B (QC; 1 trial), 7A (AB; 1 trial), 12 (BC; 1 trial) and 14 (MB; 2 trials). At each test location, a total of six broadcast foliar spray applications of the SC formulation (400 g a.i./L) were made at ~134 g a.i./ha/application with a 5 to 10-day retreatment interval for a total seasonal rates of ~806 g a.i./ha. Applications were made in ~90-449 L/ha of water using ground equipment. No adjuvant was added to the spray mixtures. Samples of potato tubers were harvested from all test sites 6-8 days following the last application. Additional samples were collected from three trials at 0, 13/14, and 20/21 days following the last application to evaluate residue decline. At each of the three trials used for residue decline, side-by-side bridging studies were conducted with the 50% WP (wettable powder) formulation.

The results from the potato field trials show that residues of fluoxastrobin (sum of E and Z isomers) were less than or at the method LOQ (≤0.01 ppm) in/on tubers harvested 6-8 days following the last of six broadcast foliar applications of fluoxastrobin at a total seasonal rate of 784-829 g a.i./ha/season.

In the residue decline studies, residues of fluoxastrobin were less than the method LOQ (<0.01 ppm) in all tuber samples from all sampling intervals following treatment with either the suspension concentrate formulation or 50% WP formulation, except one sample treated with the 50% WP formulation which bore residues at 0.0135 ppm at the 7-day PHI. The data from the three side-by-side field trials demonstrated that use of either the or 50% WP formulation will yield residues of fluoxastrobin (E and Z isomers) close to or below the LOQ in/on potato tubers.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Potato tuber (from SC formulation)	784-829	6-8	27	<0.01	<0.01	<0.01	<0.01	<0.01	0
Potato tuber (from WP formulation)	795-806	6-7	3	<0.01	<0.01	<0.01	<0.01	<0.01	0

CROP FIELD TRIALS and Residue Decline on Tomato and pepper **PMRA# 1737122**

A total of 21 field trials were conducted on tomato and peppers during the 2000 growing season. Six bell pepper trials were conducted in Regions 2 (GA; 1 trial), 3 (FL; 1 trial), 5 (KS; 1 trial), 6 (TX; 1 trial), 10 (CA; 2 trials) and 3 non-bell pepper trials were conducted in Regions 8 (TX; 1 trial), 9 (AZ; 1 trial), and 10 (CA; 1 trial). Twelve tomato trials were conducted in Regions 1 (PA; 1 trial), 2 (GA; 1 trial), 3 (FL; 2 trials), 5 (IN; 1 trial), and 10 (CA; 7 trials). At each test location, a total of four broadcast foliar spray applications of the suspension concentrate formulation (SC, 400 g/L) were made at ~202 g a.i./ha/application with a 5 to 9-day retreatment interval, for a total seasonal rates of ~806 g a.i./ha. A second side-by-side plot in six trials (three tomato and three pepper trials) was treated in the same manner with a 50% WP formulation. Applications were made in ~46-140 L of water/ha using ground equipment; no adjuvant was added to the spray mixtures. Samples of mature pepper and tomato fruits were harvested from all test sites 2-4 days following the last application. Additional samples were collected from two tomato and two pepper trials 0, 7/9, and 14/16 days following the last application of the SC or WP formulation to evaluate residue decline.

Residues of fluoxastrobin (sum of E and Z isomers) were 0.0447-0.535 ppm in/on peppers and 0.0639-0.636 ppm in/on tomatoes harvested 2-4 days following the four broadcast foliar applications of the SC formulation at total seasonal rates of 795-840 g a.i./ha. The data from the three side-by-side field trials indicate that no significant differences in the residue levels resulting from the use of the SC or the 50% WP formulations. In the side-by-side trials, residues of fluoxastrobin (sum of E and Z isomers) were 0.0985-0.376 ppm in/on peppers and 0.0253-0.233 ppm in/on tomatoes harvested 3 days following the last of four broadcast foliar applications of the 50% WP formulation at total seasonal rates of 806-829 g a.i./ha. Residues of fluoxastrobin were 0.094-0.390 ppm in/on peppers and 0.064-0.288 ppm in/on tomatoes from the respective side-by-side plots treated with the SC formulation.

In the residue decline studies, residues of fluoxastrobin (sum of E and Z isomers) declined in/on pepper and tomato samples with increasing PHIs from 0 to 14 days following treatment with either the SC or 50% WP formulation.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Bell peppers (from SC formulation)	795-840	2-4	6	0.0472	0.384	0.384	0.0924	0.138	0.13
Non-bell peppers (from SC formulation)			3	0.115	0.482	0.482	0.244	0.280	0.19
Peppers (bell and non-bell) (from WP formulation)	806-818	3	3	0.128	0.375	0.375	0.14	0.214	0.08
Tomatoes (from SC formulation)	795-818	2-4	12	0.0668	0.455	0.455	0.206	0.203	0.10
Tomatoes (from WP formulation)	806-829	3	3	0.0341 5	0.215	0.215	0.126	0.125	0.05

CROP FIELD TRIALS and Residue Decline on Strawberry | **PMRA# 1737123**

A total of eight field trials were conducted in the US in Regions 1 (PA, 1 trial), 2 (NC, 1 trial), 3 (FL, 1 trial), 5 (MI, 1 trial), 10 (CA, 3 trials), and 12 (OR, 1 trial) during the 2007 growing season. At each test location, the treated plots received four foliar broadcast applications of a SC formulation of fluoxastrobin (40.3% SC) at 200 g a.i./ha beginning 21 days prior to harvest with a 7-day RTI and a spray volume that ranged from 662-696 L/ha. Samples of strawberries were harvested at maturity on the day of the last application (0-day PHI). One site also collected decline samples at 3, 7, and 14 DALA. A non-ionic surfactant typical for the use and each region was included in the spray mix solution at 0.125-0.5% (v/v).

The results from these trials show that combined residues (sum of E and Z isomers) ranged from 0.177-1.02 ppm after four applications of fluoxastrobin at a total application rate of 800 g a.i./ha. Residue decline data show that fluoxastrobin residues decrease in/on strawberries with increasing PHIs from 0 to 14 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Fluoxastrobin Residues (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Strawberry	800	0	8	0.183	0.984	0.984	0.613	0.556	0.27

STORAGE STABILITY (RAC and the Processed Commodities) | **PMRA # 1692334, 1737120**

The storage stability data indicated that residues of fluoxastrobin (sum of E and Z isomers) were confirmed to be stable in wheat (forage, grain and straw), potato (tuber), tomato (fruit), and lettuce (head) for at least 30 months when stored at -18ºC or below. Although the recoveries in potato tuber were consistent below 70% (even at time 0 day), the low recoveries in potato tuber were likely due to extraction difficulties, rather than residue degradation.

The storage stability of fluoxastrobin (sum of E and Z isomers) in tomato, mustard greens, peanut nutmeat, potato tuber, potato chips, soybean seed, and wheat straw, hay, and grain were also conducted in a separate study. It was confirmed that fluoxastrobin residues (sum of E and Z isomers) were stable under the frozen storage conditions for up to ~1.5 months in potato chips, ~21 months in soybean, ~22 months in mustard, tomato, wheat grain, hay, and straw, and ~23 months in peanut and potato.

The freezer storage stability data in five diverse crops cover the longest frozen storage intervals in the crop field trials for matrices of pepper (13.7 months), tomato (14.5 months), corn (5.9 months), potato (12.3 months), wheat (5 months), strawberry (3.8 months), soybean (4.9 months), sweet corn (3.8 months), barley (4 months) and celery (12.9 months). Since the freezer storage stability of fluoxastrobin was demonstrated in five diverse crops (lettuce/celery (high water), soybean (high oil), peanut (high protein), potato (high starch) and tomato (high acid)) for up to 30 months, the frozen storage stability data for processed commodities are not needed.

PROCESSED FOOD AND FEED (Wheat) | **PMRA# 1692459**

Following two foliar broadcast applications of the SC formulation of fluoxastrobin at a total rate of ~1350 g a.i./ha/season, residues of fluoxastrobin (sum of E and Z isomers) were 0.09-0.11 ppm in grain, 0.09-0.18 ppm in bran, 0.01-0.02 ppm in flour, <0.01-0.06 ppm in middlings, 0.03-0.09 ppm in shorts, 0.05-0.06 ppm in germ, and 33.01-73.63 ppm in AGF.

Based on the results of the wheat processing study, residues of fluoxastrobin do not concentrate in flour, middlings, shorts or germ (average processing factors of 0.2x, <0.3x, 0.6x, and 0.6x, respectively). Residues concentrated in AGF (average processing factor of 518x), and concentrate slightly in bran (average processing factor of 1.3x).

PROCESSED FOOD AND FEED (Barley) | **PMRA# 1692448**

Following two foliar broadcast applications of the SC formulation of fluoxastrobin with an adjuvant at 0.2% (v/v) at a total rate of ~1350 g a.i./ha/season, residues of fluoxastrobin (sum of E and Z isomers) were 0.032 ppm in barley grain. The processing factor was determined to be 0.3x for pearled barley, bran and flour. A processing factor of 5.7 was determined for fluoxastrobin residues in barley hulls/husks.

PROCESSED FOOD AND FEED (Potato) | **PMRA# 1737158**

The results indicate that following a seasonal application rate of 4032 g a.i./ha, residues were 0.0248 ppm in unwashed potato. The processing data indicate that residues of fluoxastrobin (sum of E and Z isomers) concentrate slightly in wet peel (l.3x), but do not concentrate in potato granules, chips, washed and cooked tubers (<0.4x, <0.2x, <0.2x and <0.lx, respectively).

PROCESSED FOOD AND FEED (Tomato)	**PMRA# 11737157**
The results indicate that following a seasonal application rate of 4043 g a.i./ha, residues in/on tomato were 0.296 ppm. The processing data indicate that residues of fluoxastrobin (sum of E and Z isomers) concentrate in tomato paste (2.4x) and dried tomato (9.4x), but do not concentrate in tomato puree (0.8x), washed tomatoes (0.6x), hot crushed tomatoes (0.6x), and canned tomatoes (0.1x).	
LIVESTOCK FEEDING – Dairy Cattle	**PMRA # 1692462**
Lactating dairy cows were administered fluoxastrobin at a target dose level of 5.55 ppm, 28.49 ppm and 90.67 ppm in the feeds for 29 consecutive days. The dose levels of 5.55, 28.49 and 90.67 ppm represent 1.0x, 5.2x, and 16.6x, respectively, the estimated more balanced dietary burden (MBDB) to beef cattle and 0.8x, 4.0x, and 12.6x, respectively, the estimated MBDB to dairy cattle.	
LIVESTOCK FEEDING – Laying Hen	**PMRA # 1916392**
A waiver request for livestock feeding study in laying hen was submitted. Based on the calculated more balanced dietary burden for poultry (0.05 ppm), the anticipated residues in poultry liver were calculated to be ~0.0025 ppm, which is lower than the LOQ (0.02 ppm for combined residues). Thus, additional feeding study on hens is not expected to provide more scientific evidence for regulatory purpose. The waiver request for laying hen feeding study is considered acceptable.	

Commodity	Feeding level (ppm)	Highest Residues (ppm)	Dairy Cattle More Balanced Diet (ppm)	Anticipated Residue (ppm)
Milk	90.67	<0.0427	7.18	0.0034
Skim milk	90.67	<0.02		0.0016
Milk fat	90.67	<0.2009		0.114*
Liver	28.49	0.1037		0.026
Kidney	5.55, 28.49, 90.67	Regression analysis y=0.0064x+0.0217		0.068
Muscle	28.49	0.0514		0.013
Fat	28.49	0.1578		0.040

Proposed Maximum Residue Limits

Commodity	Proposed MRL (ppm)
Dried tomatoes	4.5
Crop Subgroup 4B (Leaf Petioles)	4.0
Crop Subgroup 13-07G (Low Growing Berry)	1.9
Tomato paste	1.5
Crop Group 8-09 (Fruiting Vegetables)	1.0
Corn oil	0.50
Soybean oil	0.40
Meat by-products of cattle, goat, horse, and sheep	0.20
Milk fat	0.15
Wheat bran	0.15
Crop Group 15 (Cereal Grains), except field corn, sweet corn, and popcorn	0.10
Fat of cattle, goat, horse, and sheep	0.10
Meat of cattle, goat, horse, and sheep	0.05
Dry soybeans	0.05
Eggs	0.02
Field corn	0.02
Popcorn grain	0.02
Fat, meat, and meat by-products of hogs and poultry	0.02
Milk	0.02
Crop Subgroup 1C (Tuberous and Corm Vegetables)	0.01
Sweet corn kernels plus cob with husks removed	0.01

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT		Fluoxastrin (sum of E and Z isomers)	
RESIDUE DEFINITION FOR RISK ASSESSMENT		Fluoxastrin (sum of E and Z isomers)	
METABOLIC PROFILE IN DIVERSE CROPS		Wheat, Peanut and Tomato	
ANIMAL STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT		Fluoxastrobin (sum of E and Z isomers) and the metabolite HEC7154	
RESIDUE DEFINITION FOR RISK ASSESSMENT		Fluoxastrobin (sum of E and Z isomers) and the metabolite HEC7154	
METABOLIC PROFILE IN ANIMALS		The metabolic profile is similar in goat, hen and rat.	
FAT SOLUBLE RESIDUE		No	
DIETARY RISK FROM FOOD ONLY			
Basic chronic non-cancer dietary risk **ADI = 0.015 mg/kg bw/day** **No acute reference dose (ARfD) established.** **EEC = 164 µg a.i./L (Level I, 90th percentile of yearly groundwater)**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
	All infants < 1 year	12.5	34.1
	Children 1–2 years	35.3	45.1
	Children 3 to 5 years	31.3	40.5
	Children 6–12 years	21.3	27.6
	Youth 13–19 years	13.6	18.4
	Adults 20–49 years	12.6	18.8
	Adults 50+ years	12.2	18.6
	Females 13 to 49 yrs	12.1	18.3
	Total population	15.1	21.7

Table 7 Physical and Chemical Properties of Technical Fluoxastrobin

Property	Result	Comment
Vapour pressure at 20°C	5.63×10^{-10} Pa (20°C) 8.72×10^{-10} Pa (25°C)	Low potential for residues on fruits and foliage to decrease as a result of volatilization
Henry's law constant at 20°C	1.01×10^{-7} Pa x m^3/mole (20°C)	Not volatile from water and moist soil
Ultraviolet (UV)/visible spectrum	λmax = 250 nm	Not expected to undergo phototransformation under environmental conditions.
Solubility in water at 20°C mg/L	2.56 (unbuffered) 2.43 (at pH 4) 2.29 (at pH 7) 2.27 (at pH 9)	Low solubility in water.
Solubility (g/L) in organic solvents (temperature not specified)	n-Heptane: 0.04 g/L Xylene: 38.1 g/L Dichloromethane: >250 g/L 2-Propanol: 6.7 g/L 1-Octanol: 1.09 g/L Polyethyleneglycol: 118.5 g/L Acetone: >250 g/L Ethylacetate: > 250g/L Acetonitrile: >250 g/L Dimethylsulfoxide: >250g/L	In general, soluble to very soluble in organic solvent.
n-Octanol/water partition coefficient (K_{ow})	log K_{OW}: 2.86 ± .01	Potential for bioaccumulation
Dissociation constant	Not applicable	No acidic or basic properties in water between pH 4 and 9.
Stability (temperature, metal)	Stable for one year under commercial storage in HDPE bottles.	

Table 8 Summary of maximum formation of major transformation products (Percent Applied Radioactivity) in fluoxastrobin laboratory studies at the observed day after treatment

Study conditions		Study duration [days]	Temp. [°C]	Max. Form. Fluoxastrobin-deschlorophenyl (%AR), [DAT]	Max. Form. Fluoxastrobin-carboxylic acid (%AR), [DAT]	Max. Form. Fluoxastrobin-oxazepine (%AR), [DAT]	Max. unextractable residues (%AR), [DAT]	PMRA Reference
Hydrolysis		7	50	ND (stable to hydrolysis)	ND (stable to hydrolysis)	ND (stable to hydrolysis)	NR	1692329
Phototransformation on soil Georgia (loamy sand)		15	20	ND	ND	ND	8.3[15]	1692333
Phototransformation in water		8	25	ND	ND	23.6 [8]	NR	1692338
Aerobic Soil								
Leacher Hof AXXa sandy loam		120	20	23.1[30]	ND	ND	71[120]	1692318
Byromville (loamy sand)		365	20	19.1 [270]	ND	ND	24.5[365]	1692323
Hoefchen (silt)		120	20	32.2[30]	ND	ND	58.0[120]	
Laacherhof AII (silt loam)		120	20	28.4[91]	ND	ND	39.2[120]	
Aerobic Water/sediment								
pond water-loam	Water	122	20	2.6[122]	ND	ND	NR	1692418
	Sediment			1.4[60]	ND	ND	12.7[122]	
lake water-lamy sand	Water	122	20	15.9[122]	ND	ND	NR	
	Sediment			2.4[122]	ND	ND	12.1[122]	
Anaerobic Water/sediment								
pond water-sandy clay	Water	360	20	ND	10.6[360]	ND	NR	1692421
	Sediment			ND	11.3[240]	ND	36.2[360]	

AR = Applied radioactivity, DAT = Days after treatment, ND = Not detected, NR = Not relevant

Table 9 Fate and behaviour of fluoxastrobin and its transformation products in the terrestrial and aquatic environment

Study	Test substance	Study conditions	Value[a,b]	Comments	Reference
Abiotic transformation					
Hydrolysis	Fluoxastrobin	50°C, pH 4, 7, 9	Could not be determined	Stable	1692329
Phototransformation on soil	Fluoxastrobin	20°C, loamy sand	DT_{50} = 318 d (environmental)	Not a route of transformation	1692333
Phototransformation on water	Fluoxastrobin	25°C, pH 7	DT_{50} = 27.7 d (environmental)	Possible route of transformation in shallow clear water only	1692338
Biotransformation					
Biotransformation in aerobic soil	Fluoxastrobin	Leacher Hof AXXa, (sandy loam), 20°C, 120d	DT_{50} = 18.5 d, DT_{90} = 74.7 d (DFOP) Representative $t_{1/2}$ = 22.5 d (IORE DT_{90} x 0.301)	Slightly persistent	1692318
		Byromville (loamy sand), 20°C, 365d	DT_{50} = 329 d, DT_{90} = 1479 d (DFOP) Representative $t_{1/2}$ = 495 d (DFOP slow $t_{1/2}$)	Persistent	1692323
		Hoefchen (silt), 20°C, 120d	DT_{50} = 11.2 d, DT_{90} = 53.4 d (DFOP) Representative $t_{1/2}$ = 16.1 d (IORE DT_{90} x 0.301)	Slightly persistent	
		Laacherhof AII (silt loam)	DT_{50} = 46.7 d, DT_{90} = 155 d (SFO)	Moderately persistent	
	Fluoxastrobin-carboxylic acid	Laacherhof AIII (silt loam)	DT_{50} = 21.7 d, DT_{90} = 71.9 d (SFO)	Slightly persistent	1692351
		Laacher Hof AXXa (sandy loam)	DT_{50} = 24.5 d, DT_{90} = 81.2 d (SFO)	Slightly persistent	

Study	Test substance	Study conditions	Value[a,b]	Comments	Reference
		Hofchen am Hohenseh 4a (silt)	DT_{50} = 10.9 d, DT_{90} = 36.3 d (SFO)	Non-persistent	
Biotransformation in aerobic water/sediment	Fluoxastrobin	pond water-loam, 20°C, 122d	Water: DT_{50} = 1.98 d, DT_{90} = 30.3 d (IORE) Representative $t_{1/2}$ = 9.13 d (IORE DT_{90} x 0.301)	Non-persistent	1692418
			Total system: DT_{50} = 254 d, DT_{90} = 1142 (DFOP) Representative $t_{1/2}$ = 382 d (DFOP slow $t_{1/2}$)	Persistent	
		lake water-loamy sand, 20°C, 122d	Water: DT_{50} = 4.87 d, DT_{90} = 230 d (DFOP) Representative $t_{1/2}$ = 69.3 d (DFOP slow $t_{1/2}$)	Moderately persistent	
			Total system: DT_{50} = 161 d, DT_{90} = 690 (DFOP) Representative $t_{1/2}$ = 228 d (DFOP slow $t_{1/2}$)	Persistent	
Biotransformation in anaerobic water/sediment	Fluoxastrobin	White Lake, SD (sand sediment), 25°C	Water: DT_{50} = 19.3 d, DT_{90} = 478 d (DFOP) Representative $t_{1/2}$ = 210 d (DFOP slow $t_{1/2}$)	Persistent	1672421

Study	Test substance	Study conditions	Value[a,b]	Comments	Reference
			Total system: DT_{50} = 130 d, DT_{90} = 1566 d (IORE) Representative $t_{1/2}$ = 471 d (IORE DT_{90} x 0.301)	Non-persistent	
Mobility					
Adsorption	Fluoxastrobin	Laacher Hof AXXa sandy loam	K_{OC} = 735.5 L/kg	Low	1871292
		Höfchen am Hohenseh 4a silt	K_{OC} = 874.7 L/kg	Low	
		Stanley silty clay loam	K_{OC} = 1913 L/kg	Low	
		Byromville loamy sand	K_{OC} = 541.3 L/kg	Low	
	Fluoxastrobin-deschlorophenyl	Laacher Hof AXXa sandy loam	K_{OC} = 12.98 L/kg	Very high	1871316
		Höfchen am Hohenseh 4a silt	K_{OC} = 20.46 L/kg	Very high	
		Stanley silty clay loam	K_{OC} = 180 L/kg	Low	
		Byromville loamy sand	K_{OC} = 21.35 L/kg	Very high	
	Fluoxastrobin-carboxylic acid	BBA 2.2 (loamy sand)	K_{OC} = 58.73 L/kg	High	1692384
		Laacher Hof AXXa (sandy loam)	K_{OC} = 64.56 L/kg	High	
		LUFA Speyer sandy loam	K_{OC} = 38.95 L/kg	Very high	
		Stanley silty clay	K_{OC} = 96.42 L/kg	High	
Field studies[c]					
Field dissipation	Fluoxastrobin	Prince Edward Island, Ecoregion 8.1.9	DT_{50} = 177, DT_{90} = 816 (IORE) Representative $t_{1/2}$ =246 (IORE DT_{90} x 0.301)	Persistent; Z-isomer: 18%, M48 FXA-deschlorophenyl: 4%; M40 FXA-carboxylic acid: 1%	1737161

Study	Test substance	Study conditions	Value[a,b]	Comments	Reference
		Manitoba, Ecoregion 9.2.1	DT_{50} = 333 DT_{90} = 1107 (SFO)	Persistent; Z-isomer: 9%, M48 FXA-deschloropheny l: 4%	1737160
		Washington, Ecoregion 10.1.2	DT_{50} = 363 DT_{90} = 1207 (SFO)	Persistent; Z-isomer: 3%, M48 FXA-deschloropheny l): 6%	1737165
		New York (turf), Ecoregion 8.1.1	DT_{50} = 341 DT_{90} = 1134 (SFO)	Persistent; Z-isomer: 8%, M48 FXA-deschloropheny l: 11%; M40 FXA-carboxylic acid: 1%	1737164
		New York, Ecoregion 8.1.1	DT_{50} = 258 DT_{90} = 856 (SFO)	Persistent; Z-isomer: 10%, M48 FXA-deschloropheny l: 2%	1737163
		New York, Ecoregion 8.1.1	DT_{50} = 502 DT_{90} = 1668 (SFO)	Persistent; Z-isomer: 8%, M48 FXA-deschloropheny l: 2%	1737162

[a] Kinetics models: DFOP = Double first-order in parallel; SFO = single first-order; IORE = indeterminate order rate equation.
[b] Representative $t_{1/2}$: Used by the PMRA for laboratory biotransformation studies to approximate a pseudo first-order $t_{1/2}$ from non-linear two compartment regression models.
[c] relative molar concentration of transformation products are provided in comments (% parent concentration)

Table 10 Screening level EECs for fluoxastrobin in soil and on plants based on direct application

Parameter	Crop	
	Turf	Potatoes
Application rate (g a.i./ha)	480	133.4
No. of applications	4	6
Interval between applications (days)	14	7
Soil half-life (days)[a]	502	502
Foliar half-life (days)[b]	10	10
Soil bulk density (g/cm^3)	1.5	1.5
Soil depth (cm)	15	15
Cumulative application rate to plants (g a.i./ha)	**757**	**328**
Cumulative application rate to soil (g a.i./ha)	**1866**	**781**
EEC_{soil} (mg a.i./kg soil dw)	**0.8291**	**0.3474**

[a]Based on longest DT_{50} from aerobic soil studies or field half-life (New York field study).
[b]Default 10 d foliar half-life for estimating cumulative application to plants.

Table 11 Screening level EECs for fluoxastrobin in vegetation and insects after a direct application at the cumulative application rate of 757 g a.i./ha (application to turf)

Matrix	EEC (mg a.i./kg fw) [a]	Fresh/Dry weight ratios	EEC (mg a.i./kg dw)
Short range grass	162.0027	3.3 b	534.61
Leaves and leafy crops	91.5978	11 b	1007.58
Long grass	74.1865	4.4 b	326.42
Forage crops	91.5978	5.4 b	494.63
Small insects	39.3643	3.8 c	149.58
Pods with seeds	9.8411	3.9 c	38.38
Large insects	9.8411	3.8 c	37.40
Grain and seeds	9.8411	3.8 c	37.40
Fruit	9.8411	7.6c	74.79

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973)
[b] Fresh / dry weight ratios from Harris (1975)
[c] Fresh / dry weight ratios from Spector (1956)

Table 12 Screening level EECs for fluoxastrobin in water

Use Scenario	EEC (mg a.i./L)	
	Non-permanent / shallow water bodies (15 cm)	Permanent water bodies (80 cm)
Turf (4 x 480 g a.i./ha)	1.233	0.231
Potatoes (6 x 133.4 g a.i./ha)	0.517	0.097

Table 13 Refined aquatic EECs for fluoxastrobin based on spray drift input only, assuming a 1 m distance between sprayer and aquatic habitat, at the cumulative application rate of 757 g a.i./ha (application to turf)

Sprayer Type	% Drift at 1 m (based on ASAE Medium spray quality)	EEC (mg a.i./L)	
		Non-permanent/ shallow water bodies (15 cm deep)	Permanent water bodies (80 cm deep)
Field sprayer (ground boom)	6	0.0740	0.0139

Table 14 Level 1 aquatic ecoscenario modelling EECs (µg a.i./L) for fluoxastrobin in a water body 15 cm deep, excluding spray drift.

Region	EEC (g a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Potato, 6 x 133 g a.i./ha at 7-d intervals						
Manitoba	82	59	44	41	40	36
Atlantic	99	67	47	42	42	38
Ontario	72	52	36	34	34	31
Quebec	65	49	39	38	37	35
Turf, 4 x 480 g a.i./ha at 14-d intervals						
Manitoba	53	33	19	16	16	14
Atlantic	53	32	18	16	15	13
British Columbia	46	28	16	15	15	13
Ontario	42	24	14	13	13	11
Quebec	29	18	11	9.6	9.2	8.0

Table 15 Level 1 aquatic ecoscenario modelling EECs (µg a.i./L) for fluoxastrobin in a water body 80 cm deep, excluding spray drift.

Region	EEC (g a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
Potato, 6 x 133 g a.i./ha at 7-d intervals						
Manitoba	33	32	30	30	29	26
Atlantic	38	36	32	30	30	27
Ontario	29	27	24	24	24	22
Quebec	29	28	27	27	26	25
Turf, 4 x 480 g a.i./ha at 14-d intervals						
Manitoba	16	15	13	11	11	9.6
Atlantic	15	14	12	11	11	9.6
British Columbia	14	13	12	11	11	9.6
Ontario	11	11	9.7	9.4	9.3	7.8
Quebec	9.4	8.8	7.6	6.8	6.5	5.8

Table 16 Toxicity of fluoxastrobin and major transformation products to non-target terrestrial organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Invertebrates					
Earthworm	14d-Acute	fluoxastrobin technical	LC_{50} >1000 mg/kg	n/a	1692495
Earthworm	8-weeks	Formulated fluoxastrobin (EC100)	NOEL(adult mortality, Wt gain, No. of offspring) = 1000 mg/kg	n/a	1692441
Earthworm	14d-Acute	Fluoxastrobin-carboxylic acid	LC_{50} >1000 mg/kg	n/a	1692507
Earthworm	14d-Acute	Fluoxastrobin-deschlorophenyl	LC_{50} >1000 mg/kg	n/a	1692497
Earthworm	28d	Fluoxastrobin-deschlorophenyl	NOEL(adult mortality, Wt gain, No. of offspring) = 1000 mg/kg= 1000 mg/kg	n/a	1692516
Bee	48h-Oral	fluoxastrobin technical	LD_{50} >843.3 µg a.i./bee	practically nontoxic to honey bees	1692483
	48h-Contact	fluoxastrobin technical	LD_{50} >200 µg a.i./bee	practically nontoxic to honey bees	1692483

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Predatory arthropod, ladybird beetle	17d-Contact	Formulated fluoxastrobin (EC100)	LR_{50} = 12.4 g a.i./ha	n/a	1692439
Predatory arthropod, rove beetle	17d-Contact	Formulated fluoxastrobin (EC100)	NOEL $_{(reproduction)}$ = 200 g a.i./ha	n/a	1692437
Predatory arthropod, predacious mite	7d-Contact	Formulated fluoxastrobin (EC100)	LR_{50} = 122.2 g a.i./ha	n/a	1692435
Parasitic arthropod, parasitoid wasp	48h-Contact	Formulated fluoxastrobin (EC100)	LR_{50} = 69 g a.i./ha	n/a	1692433
Birds					
Bobwhite quail	Acute	fluoxastrobin technical	LD_{50} >2000 mg a.i./kg bw	Practically nontoxic	1692312
Bobwhite quail	5d-Dietary	fluoxastrobin technical	LD_{50} >939 mg a.i./kg bw/day	Slightly toxic	1692322
Bobwhite quail	22 weeks-Reproduction	fluoxastrobin technical	NOEL: 82 mg a.i./kg bw/day	n/a	1692336
Mallard duck	5d-Dietary	fluoxastrobin technical	LD_{50} > 2195 mg a.i./kg bw/day	Practically nontoxic	1692328
Mallard duck	21 weeks - Reproduction	fluoxastrobin technical	NOEL: 53 mg a.i./kg bw/day	n/a	1692344
Mammals					
Rat	Acute		LD_{50} >2000 mg a.i./kg bw	Practically nontoxic	1692408
Rat	2-generation dietary reproductive toxicity (diet)		NOAEL(Reproductive toxicity) = 741.6 mg/kg bw/day	n/a	1692523
Vascular plants					
Vascular plant	Seedling emergence	Formulated fluoxastrobin (SC 480)	NOEC = 600 g a.i./ha	n/a	1737171
	Vegetative vigour	Formulated fluoxastrobin (SC 480)	NOEC = 600 g a.i./ha	n/a	1737171

a Atkins *et al.*(1981) for bees and USEPA classification for others, where applicable

Table 17 Toxicity of fluoxastrobin and major transformation products to non-target aquatic organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Freshwater species					
Daphnia magna	48h-Acute	fluoxastrobin technical	LC_{50} = 0.48 mg/L	Highly toxic	1692409
Gammarus pulex (most sensitive), *Daphnia gr. Galeata, Simocephalus vetulus, Acanthocyclops venustus, Chaoborus obscuripes, Cloeon dipterum, Asellus aquaticus,*	48h-Acute	fluoxastrobin technical	LC_{50} = 0.12->3.2 mg/L	Highly toxic	1692449
Daphnia magna	48h-Acute	fluoxastrobin (E:Z = 65:35)	LC_{50} = 0.87 mg/L	Highly toxic	1692409
Daphnia magna	48h-Acute	Fluoxastrobin-deschlorophenyl	LC_{50} >102 mg/L	Practically nontoxic	1692420
Daphnia magna	48h-Acute	Fluoxastrobin-carboxylic acid	LC_{50} >98 mg/L	Slighly toxic	1692417
Daphnia magna	21d-Chronic	fluoxastrobin technical	NOEC (offsprings per adult)=0.18 mg/L	n/a	1692425
Chironomus riparius	28d-Chronic	fluoxastrobin technical	NOEC (development rate) = 1 mg/L	n/a	1692472
Chironomus riparius	28d-Chronic	Fluoxastrobin-carboxylic acid	EC_{15} (emergence rate) = 98.5 mg/L	n/a	1692479
Rainbow trout	96h-Acute	fluoxastrobin technical	LC_{50} =0.435 mg/L	Highly toxic	1692354
Rainbow trout	96h-Acute	Fluoxastrobin-carboxylic acid	LC_{50} >95.7 mg/L	Slighly toxic	1692391
Rainbow trout	96h-Acute	Fluoxastrobin-deschlorophenyl	LC_{50} > 102 mg/L	Practically nontoxic	1692382
	96d-Chronic	fluoxastrobin technical	NOEC = 0.0557 mg a.i./L (highest tested concentration)	n/a	1692398
Bluegill sunfish	96h-Acute	fluoxastrobin technical	LC_{50} =0.970 mg/L	Highly toxic	1692359

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
common carp	96h-Acute	fluoxastrobin technical	LC_{50} =0.484 mg/L	Highly toxic	1692372
Vascular plant *Lemna gibba*	7d-Acute	fluoxastrobin technical	EC_{50} (frond number) = 1.2 mg/L	n/a	Not submitted to the PMRA
Freshwater algae *Selenastrum capricornutum*	96h-Acute	fluoxastrobin technical	EC_{50} (cell density)= 0.26 mg/L	n/a	1692454
Freshwater algae *Selenastrum capricornutum*	96h-Acute	Fluoxastrobin-deschlorophenyl	LOEC (cell density)= 99 mg/L	n/a	1692461
Freshwater algae *Selenastrum capricornutum*	96h-Acute	Fluoxastrobin-carboxylic acid	EC_{50} (cell density) = 110 mg/L	n/a	1692467
Marine species					
Crustacean saltwater mysid	96h-Acute	fluoxastrobin technical	LC_{50} = 0.0516 mg/L	n/a	1692434
Crustacean saltwater mysid	28d-Chronic	fluoxastrobin technical	NOEC (survival, wet weight) = 0.00061 mg/L	n/a	1692438
Mollusk Eastern Oyster	96h-Acute	fluoxastrobin technical	EC_{50} = 0.83 mg/L	n/a	1692429
Sheepshead Minnow	96h-Acute	fluoxastrobin technical	LC_{50} > 1.374 mg/L	Moderately toxic	1932519
Marine Diatom, *Skeletonema costatum*	96h-Acute	fluoxastrobin technical	EC_{50} (cell density) = 0.013 mg/L	n/a	2118508

a USEPA classification, where applicable

Table 18 Screening Level Risk to Terrestrial Organisms other than Birds and Mammals

Organism	Exposure	Endpoint value	EEC	RQ	LOC exceeded?
Red worm (*Eisenia fetida*)	14d-Acute	$LC_{50}/2$ > 500 mg a.i./kg soil	0.8291 mg a.i./kg soil	< 0.01	No
Red worm (*Eisenia fetida*)	8-weeks-Chronic	NOEL > 1000 mg a.i./kg soil	0.8291 mg a.i./kg soil	< 0.01	No
Red worm (*Eisenia fetida*)	14d-Acute	$LC_{50}/2$ > 500 mg a.i./kg soil	0.8291 mg a.i./kg soil	< 0.01	No
Red worm (*Eisenia fetida*)	14d-Acute	$LC_{50}/2$ > 500 mg a.i./kg soil	0.8291 mg a.i./kg soil	< 0.01	No

Organism	Exposure	Endpoint value	EEC	RQ	LOC exceeded?
Red worm (*Eisenia fetida*)	4-weeks-Chronic	NOEL > 1000 mg a.i./kg soil	0.8291 mg a.i./kg soil	< 0.01	No
Honey Bee (*Apis mellifera*)	48h-Acute-Oral	LC_{50} > 944 kg a.i./ha[1]	757.0 g a.i./ha	< 0.01	No
Honey Bee (*Apis mellifera*)	48h-Acute-Contact	LC_{50} > 224 kg a.i./ha[1]	757.0 g a.i./ha	< 0.01	No
Ladybird Beetle (*Coccinella septempunctata*)	17d-glass contact	LR_{50} = 12.4 g a.i./ha	757.0 g a.i./ha (in-field)	61.05	Yes
Rove Beetle (*Aleochara bilineata*)	17d-quartz sand contact	NOEL = 200 g a.i./ha	757.0 g a.i./ha (in-field)	3.79	Yes
Predatory Mite (*Typhlodromus pyri*)	7d-glass contact	LR_{50} = 122.2 g a.i./ha	757.0 g a.i./ha (in-field)	6.19	Yes
Parasitic Wasp (*Aphidius rhopalosiphi*)	48h-glass contact	LR_{50} = 69 g a.i./ha	757.0 g a.i./ha (in-field)	10.97	Yes
Ladybird Beetle(*Coccinella septempunctata*)	17d-glass contact	LR_{50} = 12.4 g a.i./ha	45.42 g a.i./ha (off-field)	3.66	Yes
Rove Beetle (*Aleochara bilineata*)	17d-quartz sand contact	NOEL = 200 g a.i./ha	45.42 g a.i./ha (off-field)	0.23	No
Predatory Mite (*Typhlodromus pyri*)	7d-glass contact	LR_{50} = 122.2 g a.i./ha	45.42 g a.i./ha (off-field)	0.37	No
Parasitic Wasp (*Aphidius rhopalosiphi*)	48h-glass contact	LR_{50} = 69 g a.i./ha	45.42 g a.i./ha (off-field)	0.66	No
Various Monocots and Dicots (Various Monocots and Dicots)	Seedling e mergence	EC_{25} > 600 g a.i./ha	757.0 g a.i./ha	< 1.26	CND[2]
Various Monocots and Dicots (Various Monocots and Dicots)	Vegetative vigour	EC_{25} > 600 g a.i./ha	757.0 g a.i./ha	< 1.26	CND[2]

[1] LD_{50} for bees foraging in treated field was calculated by multiplying laboratory LD_{50} (µg a.i./bee) x 1.12 (Atkins *et al.* 1981).
[2]CND = Could not be determined. The endpoint of concern was above the highest concentration tested. The calculated RQ represents the upper limits of our uncertainty in risk based on the proposed application rate.

Table 19 Screening Level Risk to Birds and Mammals

Exposure Type	Risk Assessment Endpoint (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute LD_{50}/10	200.00	Insectivore (small insects)	38.14	0.19
Reproduction NOEL	53.00	Insectivore (small insects)	38.14	0.72
Medium Sized Bird (0.1 kg)				
Acute LD_{50}/10	200.00	Insectivore (small insects)	29.77	0.15
Reproduction NOEL	53.00	Insectivore (small insects)	29.77	0.56
Large Sized Bird (1 kg)				
Acute LD_{50}/10	200.00	Herbivore (short grass)	31.06	0.16
Reproduction NOEL	53.00	Herbivore (short grass)	31.06	0.59
Small Mammal (0.015 kg)				
Acute LD_{50}/10	200.00	Insectivore (small insects)	21.94	0.11
Reproduction NOEL	741.60	Insectivore (small insects)	21.94	0.03
Medium Sized Mammal (0.035 kg)				
Acute LD_{50}/10	200.00	Herbivore (short grass)	68.74	0.34
Reproduction NOEL	741.60	Herbivore (short grass)	68.74	0.09
Large Sized Mammal (1 kg)				
Acute LD_{50}/10	200.00	Herbivore (short grass)	36.73	0.18
Reproduction NOEL	741.60	Herbivore (short grass)	36.73	0.05

Table 20 Screening assessment risk to aquatic organisms

Organism	Exposure	Endpoint value	EEC	RQ	LOC exceeded?
Freshwater Invertebrates					
Water Flea (*Daphnia magna*)	48h-Acute	1/2 LC_{50} = 0.24 mg a.i./L	0.2311 mg/L	0.96	No
Freshwater amphipod (*Gammarus pulex*)	48h-Acute	1/2 LC_{50} = 0.06 mg a.i./L	0.2311 mg/L	3.85	Yes
Water Flea (*Daphnia magna*)	48h-Acute	1/2 LC_{50} = 0.435 mg a.i./L	0.2311 mg/L	0.53	No
Water Flea (*Daphnia magna*)	21d-Chronic	NOEC = 0.18 mg a.i./L	0.2311 mg/L	1.28	Yes

Organism	Exposure	Endpoint value	EEC	RQ	LOC exceeded?
Midge larvae (*Chironomus riparius*)	28d-Chronic	NOEC = 1 mg a.i./L	0.2311 mg/L	0.23	No
Freshwater fish					
Rainbow trout (*Onchorynchuys mykiss*)	96h-Acute	1/10 LC_{50} = 0.0435 mg a.i./L	0.2311 mg/L	5.31	Yes
Bluegill sunfish (*Lemomis macrochirus*)	96h-Acute	1/10 LC_{50} = 0.097 mg a.i./L	0.2311 mg/L	2.38	Yes
Common carp (*Cyprinus carpio*)	96h-Acute	1/10 LC_{50} = 0.0484 mg a.i./L	0.2311 mg/L	4.78	Yes
Rainbow trout (*Onchorynchuys mykiss*)	96d-Chronic	NOEC = 0.0557 mg a.i./L	0.2311 mg/L	4.15	Yes
Freshwater plants and algae					
Duckweed (*Lemna gibba*)	7d-Acute	½ EC_{50} = 0.6 mg a.i./L	0.2311 mg/L	0.39	No
Duckweed (*Lemna gibba*)	7d-Acute	½ EC_{50} = 1.45 mg a.i./L	0.2311 mg/L	0.16	No
Green Algae (*Selenastrum capricornutum*)	96h-Acute	½ EC_{50} = 0.13 mg a.i./L	0.2311 mg/L	1.78	Yes
Amphibians (Represented by fish; EEC calculated for 15 cm depth)					
Rainbow trout (*Onchorynchuys mykiss*)	96h-Acute	1/10 LC_{50} = 0.0435 mg a.i./L	1.2327 mg/L	28.34	Yes
Bluegill sunfish (*Lemomis macrochirus*)	96h-Acute	1/10 LC_{50} = 0.097 mg a.i./L	1.2327 mg/L	12.71	Yes
Common carp (*Cyprinus carpio*)	96h-Acute	1/10 LC_{50} = 0.0484 mg a.i./L	1.2327 mg/L	25.47	Yes
Rainbow trout (*Onchorynchuys mykiss*)	96d-Chronic	NOEC = 0.0557 mg a.i./L	1.2327 mg/L	22.13	Yes
Marine Invertebrates					
Saltwater mysid shrimp (*Americamysis bahia*)	96h-Acute	½ LC_{50} = 0.0258 mg a.i./L	0.2311 mg/L	8.96	Yes
Saltwater mysid shrimp (*Americamysis bahia*)	28d-Chronic	NOEC = 0.00061 mg a.i./L	0.2311 mg/L	378.89	Yes
Eastern Oyster (*Crassostrea virginica*)	96h-Acute	½ LC_{50} = 0.415 mg a.i./L	0.2311 mg/L	0.56	No
Marine fish					
Sheapshead Minnow (*Cyprinodon variegatus*)	96h-Acute	1/10 LC_{50} > 0.1374 mg a.i./L	0.2311 mg/L	< 1.68	CND[1]

Organism	Exposure	Endpoint value	EEC	RQ	LOC exceeded?
Marine algae					
Diatom (*Skeletonema costatum*)	96h-Acute	½ EC_{50} =0.0065 mg a.i./L	0.2311 mg/L	35.56	Yes

[1]CND = Could not be determined. The endpoint of concern was above the highest concentration tested. The calculated RQ represents the upper limits of our uncertainty in risk based on the proposed application rate.

Table 21 Tier I level risk to aquatic organisms from spray drift and runoff inputs

Organism	Exposure	Endpoint value	6% srpay drift		Runoff	
			EEC	RQ	EEC	RQ
Freshwater Invertebrates						
Water Flea (*Daphnia magna*)	48h-Acute	½ LC_{50} = 0.24 mg a.i./L	0.0139 mg/L	0.06	0.038 mg/L	0.16
Freshwater amphipod (*Gammarus pulex*)	48h-Acute	½ LC_{50} = 0.06 mg a.i./L	0.019 mg/L	0.23	0.038 mg/L	0.63
Water Flea (*Daphnia magna*)	48h-Acute	½ LC_{50} = 0.435 mg a.i./L	0.0139 mg/L	0.03	0.038 mg/L	0.09
Water Flea (*Daphnia magna*)	21d-Chronic	NOEC = 0.18 mg a.i./L	0.0139 mg/L	0.08	0.032 mg/L	0.18
Midge larvae (*Chironomus riparius*)	28d-Chronic	NOEC = 1 mg a.i./L	0.0139 mg/L	0.014	0.032 mg/L	0.03
Freshwater Fish						
Rainbow trout (*Onchorynchuys mykiss*)	96h-Acute	1/10 LC_{50} = 0.0435 mg a.i./L	0.0139 mg/L	0.32	0.036 mg/L	0.83
Bluegill sunfish (*Lemomis macrochirus*)	96h-Acute	1/10 LC_{50} = 0.097 mg a.i./L	0.0139 mg/L	0.14	0.036 mg/L	0.37
Common carp (*Cyprinus carpio*)	96h-Acute	1/10 LC_{50} = 0.0484 mg a.i./L	0.0139 mg/L	0.29	0.036 mg/L	0.74

Organism	Exposure	Endpoint value	6% srpay drift		Runoff	
			EEC	RQ	EEC	RQ
Rainbow trout (*Onchorynchuys mykiss*)	96d-Chronic	NOEC = 0.0557 mg a.i./L	0.0139 mg/L	0.25	0.03 mg/L	0.54
Freshwater Plants and Algae						
Duckweed (*Lemna gibba*)	7d-Acute	½ EC_{50} = 0.6 mg a.i./L	0.0139 mg/L	0.02	0.036 mg/L	0.06
Duckweed (*Lemna gibba*)	7d-Acute	½ EC_{50} = 1.45 mg a.i./L	0.0139 mg/L	< 0.01	0.036 mg/L	0.03
Green Algae (*Selenastrum capricornutum*)	96h-Acute	½ EC_{50} = 0.13 mg a.i./L	0.0139 mg/L	0.11	0.036 mg/L	0.28
Amphibians (represented by fish endpoints, RQ, calculated in 15 cm water)						
Rainbow trout (*Onchorynchuys mykiss*)	96h-Acute	1/10 LC_{50} = 0.0435 mg a.i./L	0.0740 mg/L	1.70	0.099 mg/L	2.28
Bluegill sunfish (*Lemomis macrochirus*)	96h-Acute	1/10 LC_{50} = 0.097 mg a.i./L	0.0740 mg/L	0.76	0.099 mg/L	1.02
Common carp (*Cyprinus carpio*)	96h-Acute	1/10 LC_{50} = 0.0484 mg a.i./L	0.0740 mg/L	1.53	0.099 mg/L	2.05
Rainbow trout (*Onchorynchuys mykiss*)	96d-Chronic	NOEC = 0.0557 mg a.i./L	0.0740 mg/L	1.33	0.042 mg/L	0.75
Marine Invertebrates						
Saltwater mysid shrimp (*Americamysis bahia*)	96h-Acute	½ LC_{50} = 0.0258 mg a.i./L	0.0139 mg/L	0.54	0.036 mg/L	1.40
Saltwater mysid shrimp (*Americamysis bahia*)	28d-Chronic	NOEC = 0.00061 mg a.i./L	0.0139 mg/L	22.73	0.03 mg/L	49.18

Organism	Exposure	Endpoint value	6% srpay drift		Runoff	
			EEC	RQ	EEC	RQ
Eastern Oyster (*Crassostrea virginica*)	96h-Acute	½ LC_{50} = 0.415 mg a.i./L	0.0139 mg/L	0.03	0.036 mg/L	0.09
Marine Fish						
Sheapshead Minnow (*Cyprinodon variegatus*)	96h-Acute	1/10 LC_{50} > 0.1374 mg a.i./L	0.0139 mg/L	0.10[1]	0.036 mg/L	0.26[1]
Marine Algae						
Diatom (*Skeletonema costatum*)	96h-Acute	½ EC_{50} =0.0065 mg a.i./L	0.0139 mg/L	2.13	0.036 mg/L	5.54

[1]The endpoint of concern was above the highest concentration tested. The calculated RQ represents the upper limits of our uncertainty in risk based on the proposed application rate.

Table 22 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints
Toxic or toxic equivalent as defined by the *Canadian Environmental Protection Act*[1]	Yes		Yes. RQs for aquatic invertebrates > LOC.
Predominantly anthropogenic[2]	Yes		
Persistence[3]:	Soil	Half-life ≥ 182 days	Longest DT_{50} = 502 days
	Water	Half-life ≥ 182 days	Longest DT_{50} = 382 days
	Sediment	Half-life ≥ 365 days	Not calculated.
	Air	Half-life ≥ 2 days or	Half-life or volatilisation is not an important route of dissipation and long-range atmospheric

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints
		evidence of long range transport	transport is unlikely to occur based on the vapour pressure (5.63 x 10-10 Pa at 20°C) and Henry's Law Constant (1.01 x 10-7 Pa x m3/mole at 20°C).
Bioaccumulation[4]	Log $K_{OW} \geq 5$		Log $K_{OW} = 2.86$
	BCF ≥ 5000		Not available
	BAF ≥ 5000		Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.

[1]All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (i.e., all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Field data (example,, BAFs) are preferred over laboratory data (example,, BCFs) which, in turn, are preferred over chemical properties (example,, log K_{OW}).

Table 23 Alternative Fungicides Registered for Diseases of Crops on the Evito 480 SC Fungicide Label

Crop	Disease	Resistance Management Group	Active Ingredients
wheat / barley	stem rust	3	prothioconazole, tebuconazole
		11	trifloxystrobin
	powdery mildew	3	prothioconazole, tebuconazole, triadimenol
		11	pyraclostrobin, trifloxystrobin
corn	common rust	3	propiconazole, prothioconazole
		11	azoxystrobin, trifloxystrobin
	southern corn leaf blight	3	propiconazole
		11	azoxystrobin, pyraclostrobin
soybean	frogeye leaf spot	3	propiconazole, prothioconazole, tebuconazole
		11	azoxystrobin, pyraclostrobin, trifloxystrobin
		44	*Bacillus subtilis* strain QST 713
potato	late blight	4	metalaxyl-M and -S isomer
		11	azoxystrobin, famoxadone, pyraclostrobin
		21	cyazofamid
		22	zoxamide
		27	cymoxanil
		28	propamocarb hydrochloride
		29	fluazinam
		33	phosphorous acid (mono- and di-potassium salts)
		40	dimethomorph, mandipropamid

Crop	Disease	Resistance Management Group	Active Ingredients
		43	fluopicolide
		M1	copper (different salts)
		M3	mancozeb, maneb, metiram, zineb
		M4	captan
		M5	chlorothalonil
fruiting vegetables (including tomato and pepper)	Late blight	11	famoxadone, pyraclostrobin
		27	cymoxanil
		28	propamocarb hydrochloride
		40	mandipropamid
		43	fluopicolide
		M1	copper (different salts)
		M3	mancozeb, maneb, metiram thiram ziram
		M4	captan
		M5	chlorothalonil
strawberry	anthracnose	7	boscalid
		11	pyraclostrobin
turf	dollar spot	1	thiophanate-methyl
		2	iprodione
		3	myclobutanil, propiconazole, triticonazole
		7	boscalid
		11	azoxystrobin, pyraclostrobin
		44	*Bacillus subtilis* strain QST 713
		M	chlorothalonil

Table 24 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed label claim	Support for claim
To control frogeye leaf spot on soybean, apply Evito 480 SC Fungicide at a rate of 146-417 mL/ha up to four times per season at 14 day intervals.	Supported as proposed with a rate range of 146-296 mL/ha
To control dollar spot on turf, apply Evito 480 SC Fungicide at a rate of 585-1169 mL/ha up to four times per season at 14-21 day intervals.	Supported as proposed at a rate range of 500 – 1000 mL/ha
To control stem rust on wheat & barley, apply Evito 480 SC Fungicide at a rate of 146-292 mL/ha up to two times per season at a 14-21 day interval.	Supported as proposed.
To control powdery mildew on wheat & barley, apply Evito 480 SC Fungicide at a rate of 183-292 mL/ha up to two times per season at a 14-21 day interval.	Supported as proposed.
To control common rust on corn (field, seed, sweet) apply Evito 480 SC Fungicide at a rate of 146-417 mL/ha up to two or four times per season at seven day intervals.	Supported at the rates of 146-296 mL/ha

Proposed label claim	Support for claim
To control southern corn leaf on corn (field, seed, sweet), apply Evito 480 SC Fungicide at a rate of 146-296 mL/ha up to two or four times per season at seven day intervals.	Supported as proposed at the rates of 146-296 mL/ha
To suppress late blight on potato, apply Evito 480 SC Fungicide at a rate of 278 mL/ha up to four times per season at seven day intervals.	Supported as proposed
To suppress late blight on tomato & pepper apply Evito 480 SC Fungicide at a rate of 417 mL/ha up to four times per season at seven day intervals	Supported as proposed at the rate of 278 mL/ha
To control anthracnose on strawberry, apply Evito 480 SC Fungicide at a rate of 146-417mL/ha up to four times per season at 14 day intervals.	Supported as proposed at the rates of 146-280 mL/ha
Control of various fungal diseases on wheat, barley, corn, soybean, potato, tomato, pepper, strawberry and turf.	Insufficient information was available to support other disease claims on the crops appearing on the Evito 480 SC Fungicide label.
Control of early blight, late blight and rhizoctonia root rot on celery.	Insufficient information was available to support disease claims on celery.

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

As per Table 1, the proposed MRLs in Canada differ from the corresponding tolerances established in the United States (tolerances listed in *40 CFR Part 180* by pesticide). Codex MRLs[10] (*Codex MRLs* searchable by pesticide or commodity) have not been established for fluoxastrobin on any commodity.

Table 1 Differences Between Canadian MRLs and in Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex (ppm)
Berry, low growing (Crop Subgroup 13-07G)	1.9	1.9	Not reviewed by Codex
Cereal grains (Crop Group 15), except corn (field, sweet and popcorn)	0.10	0.10	
Field corn	0.02	0.02	
Popcorn grain	0.02	No tolerance established	
Corn oil	0.50	No tolerance established	
Sweet corn kernels plus cob with husks removed	0.01	0.01	
Leaf petioles (Crop Subgroup 4B)*	4.0	4.0	
Soybean oil	0.40	No tolerance established	
Dry soybeans	0.05	0.05	
Dried tomatoes	4.5	No tolerance established	
Tomato paste	1.5	1.5	
Fruiting vegetables (Crop Group 8-09)	1.0	1.0	
Tuberous and corm vegetables (Crop Subgroup 1C)	0.01	0.01	
Wheat bran	0.15	0.15	
Fat of cattle, goats, horses and sheep	0.10	0.10	
Meat of cattle, goats, horses and sheep	0.05	0.05	
Meat byproducts of cattle, goats, horses and sheep	0.20	0.20	
Milk	0.02	0.02	
Milk fat	0.15	0.50	
Fat, meat and meat byproducts of hogs and poultry	0.02	Exempt	
Eggs	0.02	Exempt	

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

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

Under the North American Free Trade Agreement, Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

*Celery is supported only as an import tolerance at this time.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
1692310	Product Chemistry - Fluoxastrobin Technical See PMRA # 1739839, 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 tocxicity tests by HPLC, DACO: 8.2.2.3
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
1692426 2000, Determination of HEC 5725 in formulations, DACO: 3.4.1
1737107 2009, Product Chemistry Data to Support the Registration of Evito 480 SC Fungicide, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.5.4,3.5.5 CBI
1737108 2003, Product Chemistry of HEC 480 SC Fungicide, DACO: 3.2.1,3.2.2,3.3.1,3.4.1,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2, 3.5.3,3.5.6,3.5.7,3.5.8,3.5.9 CBI
1774634 2009, Confidential Disclosure of [CBI removed], DACO: 3.2.1 CBI

2.0 Human and Animal Health

PMRA Document Number **Reference**

1692315 2001, 12 months storage stability of residues of HEC 5725 during frozen storage in/on matrices of plant origin, DACO: 7.3
1692316 2002, HEC 5725: List of Metabolites, DACO: 6.4
1692324 2002, 24 months storage stability of residues of HEC 5725 during frozen storage in/on matrices of plant origin, DACO: 7.3
1692334 2003, 30 months storage stability of residues of HEC 5725 during frozen storage in/on matrices of plant origin, DACO: 7.3
1692335 2001, Analytical determination of residues of the fungicide HEC 5725 in/on cereals, cereal processed products and vegetables by HPLC-MS/MS Method No. 00604, DACO: 7.2.1
1692337 2001, Metabolism of [methoxyiminotolyl-ring-UL-14C]HEC5725 in spring wheat, DACO: 6.3
1692343 2002, Independent laboratory validation of the ASE extraction method as described by BAYER Method 00604: Analytical determination of residues of the fungicide HEC 5725 in/on cereals, cereal processed products and vegetables by HPLC-MS/MS, DACO: 7.2.3
1692345 2001, Metabolism of [chlorophenyl-UL-14C]HEC5725 in spring wheat, DACO: 6.3
1692353 2001, Analytical Method 00649 for the determination of residues of HEC 5725 in/on matrices of plant origin by HPLC-MS/MS, DACO: 7.2.1,8.2.2.4

1692358 2002, Independent laboratory validation of the microwave extraction method as described in analytical method 00649 for the determination of residues of HEC 5725 in/on matrices of plant origin by HPLC-MS/MS, DACO: 7.2.3

1692363 2001, Metabolism of [pyrimidine-2-14C]HEC5725 in spring wheat, DACO: 6.3

1692371 2001, Enforcement Method 00668 for the determination of residues of HEC 5725 in/on matrices of plant origin by HPLC-MS/MS. Method 00668, DACO: 7.2.1,7.2.2,8.2.2.4

1692377 2002, Metabolism of [methoxyiminotolyl-ring-UL-14C]HEC5725 in peanuts, DACO: 6.3

1692378 2001, Independent laboratory validation of Method 00668 for the determination of residues of HEC 5725 in/on matrices of plant origin by HPLC-MS/MS, DACO: 7.2.3

1692383 2001, [Methoxyiminotolyl-ring-UL-14C]HEC5725: Absorption, distribution, excretion and metabolism in the lactating goat, DACO: 6.2

1692387 2002, Metabolism of [pyrimidine-2-14C]HEC5725 in peanuts, DACO: 6.3

1692388 2001, Residue analytical Method 00691 for the determination of residues of HEC 5725 (E+Z isomers) and HEC 7154 in animal tissues by HPLC with electrospray MS/MS-detection. method 00691/M001, DACO: 7.2.1,8.2.2.4

1692393 2001, [Chlorophenyl-UL-14C]HEC5725: Absorption, distribution, excretion and metabolism in the lactating goat, DACO: 6.2

1692394 2001, Independent laboratory validation of Method 00691 for the determination of residues of HEC 5725 (E+Z isomers) and HEC 7154 in matrices of animal origin by HPLC-MS/MS, DACO: 7.2.3

1692399 2001, Metabolism of [chlorophenyl-UL-14C]HEC5725 in tomatoes, DACO: 6.3

1692400 2001, [Chlorophenyl-UL-14C]HEC5725: Absorption, distribution, excretion and metabolism in laying hens, DACO: 6.2

1692402 2001, Modification and independent laboratory validation of residue analytical Method 00691 for the determination of residues of HEC 5725 (E+Z isomers) and HEC 7154 in animal tissues, DACO: 7.2.4

1692404 2001, Metabolism of [methoxyiminotolyl-ring-UL-14C]HEC5725 in tomatoes, DACO: 6.3

1692405 2001, [Methoxyiminotolyl-ring-UL-14C]HEC5725: Absorption, distribution, excretion and metabolism in laying hens, DACO: 6.2

1692407 2002, Multiresidue method testing for HEC 5725 E- and Z-isomers and HEC 7154 according to PAM I, Appendix II as updated January, 1994., DACO: 7.2.4,8.2.2.4

1692443 2008, Residue of Fluoxastrobin in/on Field Corn Process Fractions, DACO: 7.4.5

1692448 2008, Residues of Fluoxastrobin in/on Barley Process Fractions, DACO: 7.4.5

1692456 2008, Residue of Fluoxastrobin in/on Soybean Processed Fractions, DACO: 7.4.5

1692459 2008, Residue of Fluoxastrobin in/on Wheat Process Fractions, DACO: 7.4.5

1692462 2001, HEC 5725 - A 29-day dairy cattle feeding study, DACO: 7.5

1692463 2008, Residues of Fluoxastrobin in/on Wheat, DACO: 7.4.1

1692471 2008, Magnitude of the Residue of Fluoxastrobin and its Z-Isomer in/on Strawberry Raw Agricultural Commodities Following Four Foliar Applications of ARY-0473-001, DACO: 7.4.1

1692482 2001, Confined rotational crop study with [methoxyiminotolyl]-ring-UL-14C]HEC5725, DACO: 7.4.3

1692484 2001, Confined rotational crop study with [chlorophenyl-UL-14C]HEC5725, DACO: 7.4.3

1692490 2001, Confined rotational crop study with [pyrimidine-2-14C]HEC5725, DACO: 7.4.3

1737120 2002, HEC 5725 480 SC - Magnitude of Residues on Celery, DACO: 7.2.2,7.2.5,7.4.1,7.4.2

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