Proposed Registration Decision PRD2012-10

Picoxystrobin

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Overview

Proposed Registration Decision for Picoxystrobin

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 Picoxystrobin Technical Fungicide and DuPont Acapela Fungicide, containing the technical grade active ingredient picoxystrobin, to control or suppress a broad spectrum of diseases on cereals, corn, dry legumes and soybeans.

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 Picoxystrobin Technical Fungicide and DuPont Acapela Fungicide.

What Does Health Canada Consider When Making a Registration Decision?

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

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for 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 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.

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

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

Before making a final registration decision on picoxystrobin, 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 picoxystrobin, 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 Picoxystrobin?

Picoxystrobin is a fungicide active ingredient that controls or suppresses a broad spectrum of diseases in numerous crops. It has moderate uptake into host leaves through the xylem and exhibits translaminar movement.

Health Considerations

Can Approved Uses of Picoxystrobin Affect Human Health?

Picoxystrobin is unlikely to affect your health when used according to label directions.

Potential exposure to picoxystrobin 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 (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

In laboratory animals, the technical grade active ingredient picoxystrobin was of moderate acute toxicity by the inhalation route and was mildly irritating to the eyes; consequently, the hazard signal words "WARNING – POISON" and "EYE IRRITANT" are required on the label. It was of low acute toxicity orally and dermally. Picoxystrobin was non-irritating to the skin and did not cause an allergic skin reaction.

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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*.

The acute toxicity of the end-use product DuPont Acapela Fungicide, containing picoxystrobin, was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes, slightly irritating to the skin and did not cause an allergic skin reaction. No hazard signal words are required on the label.

Health effects in animals given repeated doses of picoxystrobin included irritation of the mucous membranes throughout the gastrointestinal tract (G.I. tract). Picoxystrobin did not damage genetic material or cause cancer at doses that were relevant to human risk assessment. There was no indication that picoxystrobin caused damage to the immune system. Picoxystrobin did not cause birth defects in animals and there were no effects on reproduction. When picoxystrobin was given to pregnant or nursing animals, effects on the juvenile animal (decreased spleen weight) were observed at doses lower than those that were toxic to the mother, indicating that the young may be slightly more sensitive than the adult animal.

The risk assessment protects against the effects of picoxystrobin 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 yrs), the subpopulation which would ingest the most picoxystrobin relative to body weight, are expected to be exposed to less than 3% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from picoxystrobin is not of concern for all population sub-groups. There were no cancer risks of concern.

An aggregate (food and water) dietary intake estimate for the highest exposed population (all infants, <1 year old) used less than 1% (95^{th} Percentile) of the acute reference dose, which is not a health concern.

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 *Pest Control Products Act (PCPA).* Food containing a pesticide residue at the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using picoxystrobin on corn (field and sweet), wheat, barley, soybean, dried pea, dried bean and imported canola are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Consultation Document.

Occupational Risks From Handling DuPont Acapela Fungicide

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

Farmers and custom applicators who mix, load or apply DuPont Acapela Fungicide as well as field workers re-entering recently treated fields can come in direct contact with picoxystrobin residues on the skin. Therefore, the label specifies that anyone mixing/loading and applying DuPont Acapela Fungicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves and shoes plus socks during mixing and loading and a long-sleeved shirt, long pants and shoes plus socks during application. 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, it was determine that the 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 Picoxystrobin Is Introduced Into the Environment?

Picoxystrobin can pose a risk to earthworms, beneficial predatory and parasitic arthropods, non-target terrestrial plants and freshwater aquatic invertebrates, fish, amphibians and algae; therefore, statements on the product label are required to inform users of the potential risks, and spray buffer zones are required during application.

When picoxystrobin is applied as a fungicide in field crops, some of the active ingredient finds its way into soil and water. Picoxystrobin has low solubility in water and will partition to sediments. Picoxystrobin is broken down by microbial activity in soil, sediment and water; thus, it is not expected to persist in the environment. Four major transformation products (Compounds 2, 3, 7 and 8) may be present in soil or aquatic systems for a longer period of time. Compound 26 is a volatile transformation product formed in soil. Laboratory and field studies indicate that picoxystrobin and its transformation products have low mobility in soil and have low potential to leach to groundwater, except for one transformation product at one field site where precipitation levels were very high. Picoxystrobin and its transformation products are not expected to carry over in important amounts into the next growing season. Picoxystrobin does not appreciably bioconcentrate in fish. Picoxystrobin is not volatile and therefore not expected to be subject to long-range transport in the atmosphere. There is some uncertainty as to the persistence and potential for long-range transport of Compound 26, a major volatile transformation product formed in soil.

Picoxystrobin can be applied by field sprayer or aerial application. 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. Picoxystrobin is not expected to pose a risk to bees, birds, small mammals, freshwater

vascular plants and marine/estuarine organisms at the proposed use rates. Picoxystrobin exposure can present a risk to earthworms, beneficial predatory and parasitic arthropods, terrestrial plants, and freshwater invertebrates, fish, amphibians and algae; therefore, statements on the product label are required to inform users of the potential risks. 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. No environmental risk was identified from exposure to the major transformation products of picoxystrobin.

Value Considerations

DuPont Acapela Fungicide is a broad-spectrum fungicide with locally systemic activity for control of foliar plant diseases.

DuPont Acapela Fungicide controls or suppresses primary diseases of major field crops grown in Canada and can be integrated into a spray program as a rotational product or tank mix partner.

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 DuPont Acapela Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

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

The label must also include the following restrictions:

1. If wheat forage will be harvested, make only one application.
2. If soybean forage and hay will be harvested, make only one application.
3. All other crops not on the label may be planted after 10 months following the last application of picoxystrobin.

Environment

Picoxystrobin can pose a risk to earthworms and beneficial predatory and parasitic arthropods when used in Integrated Pest Management strategies. Label statements informing the users of the potential risks to these organisms are specified on the product label.

Spray drift of picoxystrobin can pose a risk to non-target terrestrial vascular plants, freshwater aquatic invertebrates, fish, amphibians and algae. To mitigate potential exposures via spray drift, spray buffer zones of 1 to 2 metres are required to protect sensitive terrestrial habitats, and spray buffer zones of 1 to 35 metres, depending on the type of application equipment and the crop, are required to protect sensitive aquatic habitats. These spray buffer zones are specified on the product label.

Next Steps

Before making a final registration decision on picoxystrobin, 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

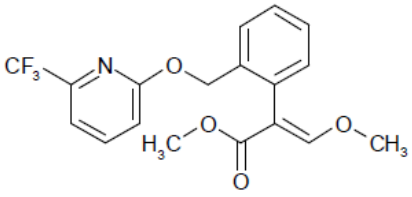
When the PMRA makes its registration decision, it will publish a Registration Decision on picoxystrobin (based on the Science Evaluation section of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application,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

Science Evaluation

Picoxystrobin

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Picoxystrobin
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Methyl (2*E*)-3-methoxy-2-{2-[6-(trifluoromethyl)-2-pyridyloxymethyl]phenyl}acrylate
2. Chemical Abstracts Service (CAS)	Methyl (α*E*)-α-(methoxymethylene)-2-[[[6-(trifluoromethyl)-2-pyridinyl]oxy]methyl]benzeneacetate
CAS number	117428-22-5
Molecular formula	$C_{18}H_{16}F_3NO_4$
Molecular weight	367.3 g/mol
Structural formula	
Purity of the active ingredient	98%

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

Technical Product—Picoxystrobin Technical Fungicide

Property	Result
Colour and physical state	Cream solid
Odour	No characteristic odour
Melting range	Pure material: 71.9 – 74.3°C Technical material: 75.0°C
Boiling point or range	Not applicable for a solid
Density at 20°C	1.40 g/cm^3
Vapour pressure at 20°C	5.5×10^{-3} mPa

Property	Result
Henry's law constant at 20°C	6.13 x 10^{-9} atm·m^3/mol
Ultraviolet (UV)-visible spectrum	In methanol, maxima were observed at 209.6 nm, 218.1 nm and in the range of 234.4 to 244.5 nm. Not expected to absorb at λ > 300 nm
Solubility in water at 20°C	3.1 mg/L
Solubility in organic solvents at 20°C (g/100 mL)	Solvent / Solubility (g/L / g/kg) xylene >200 250 1,2-dichloromethane " " acetone " " ethyl acetate " " n-heptane 4 6 methanol 79 96
n-Octanol-water partition coefficient (K_{ow})	log K_{ow} = 3.6
Dissociation constant (pK_a)	The dissociation constant of the active is that of an extremely weak base, calculated to be less than 1, and therefore cannot be measured.
Stability (temperature, metal)	Stable for two weeks at elevated (54ºC) temperature, and in contact with iron and aluminum metals and their acetate salts.

End-Use Product—DuPont Acapela Fungicide

Property	Result
Colour	Off-white
Odour	No characteristic odour
Physical state	Liquid
Formulation type	Suspension
Guarantee	250 g/L
Container material and description	Metal, glass and plastic jug or tote of size ranging from 1 L to 2500 L.
Density	1.107 g/mL at 20ºC
pH of 1% dispersion in water	7.22 at 25ºC
Oxidizing or reducing action	The product does not contain any oxidizing or reducing agents.
Storage stability	Stable for 12 months in HDPE packaging.
Corrosion characteristics	Not corrosive to HDPE packaging.
Explodability	Not explosive.

1.3 Directions for Use

Cereals: Apply DuPont Acapela Fungicide to cereal crops prior to disease onset (at Feeke's stage 9 or 'flag leaf out' stage) at rates ranging between 0.44 – 0.88 L/ha (110 – 225 g a.i./ha). Repeat applications may be made at 7 – 10 day intervals, but should not be applied after flowering (Feeke's stage 10.5).

Corn: Apply DuPont Acapela Fungicide to corn prior to disease onset at rates ranging between 0.53 – 0.88 L/ha (132.5 – 225 g a.i./ha). Applications should begin at the bud to early flowering stage. Repeat applications may be made at 7 – 14 day intervals. The product may be applied with a non-ionic surfactant.

Dry Legumes: Apply DuPont Acapela Fungicide to dry legumes prior to disease onset at rates ranging between 0.60 – 0.88 L/ha (150 – 225 g a.i./ha). Repeat applications may be made at 7 – 10 day intervals. When treating for ascochyta blight, DuPont Acapela Fungicide must be tank mixed with another registered fungicide with a different mode of action. No more than two applications may be made to target this disease.

Soybeans: Apply DuPont Acapela Fungicide to soybeans prior to disease onset at rates ranging between 0.44 – 0.88 L/ha (110 – 225 g a.i./ha). Repeat applications may be made at 7 – 14 day intervals. For white mould, the first application should be made at 100% bloom (one flower blooming on all plants). A second application may be made 7 – 10 days later at full bloom.

The recommended water volume for ground application to all crops is a minimum of 110 L/ha. Acapela Fungicide may be applied by air to all labelled crops using a minimum application volume of 50 L water/ha.

1.4 Mode of Action

Picoxystrobin is a quinone outside inhibitor (QoI) fungicide that inhibits mitochondrial respiration.

Picoxystrobin fungicide provides control of target fungi by blocking spore germination and inhibiting germ tube formation and mycelial growth. Picoxystrobin also induces spore collapse and death.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

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

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

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

The LC-MS/MS (liquid chromatography with tandem mass spectrometry) methods (Method#s Du-Pont-29312 and Du-Pont-25997, Revision No. 1) 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 Du-Pont-29312 and Du-Pont-25997, Revision No. 1) were successfully validated by an independent laboratory. 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 picoxystrobin 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 picoxystrobin.

Picoxystrobin is a member of the strobilurin class of pesticides. This class of pesticides impairs energy function in the mitochondria.

In single-dose rat oral metabolism studies, radiolabelled picoxystrobin was rapidly absorbed with peak blood concentrations (T_{max}) between 0.5-1.0 hours at low doses and at 24 hours at high doses. The presence of two peaks of radioactivity in the blood indicated an enterohepatic circulation of metabolites, which was supported by the results of bile cannulation studies. The elimination half-life ($T_{1/2elim}$) was similarly rapid and ranged between 30.5-47.2 hours at both low and high doses. Absorption was extensive at 77-82% of the administered dose, elimination was primarily via the bile and excretion was complete (94-100%). In plasma kinetics, there was a general similarity between sexes, radiolabel location and dose groups, though there was a high degree of variability between individual rats. The only difference between the sexes was a slightly higher area under the curve in low dose males than females; however, there is little to no difference in high-dose animals. Differences between the high and low doses indicated a possible saturation of the metabolic pathways. There was no evidence of bioaccumulation. The highest levels of radioactive residues were in the G.I. tract, kidneys and liver at 24 hours post-dose. At

120 hours post-dose, the liver had the highest concentrations of residual radioactivity, followed by the kidneys and G.I. tract. Picoxystrobin was extensively metabolized and well characterized. The major route of metabolism was via ester hydrolysis and glucuronide conjugation.

Following acute dosing, picoxystrobin was found to be of low oral and dermal toxicity in rats. It was moderately acutely toxic to rats via the inhalation route. It was mildly irritating to the eyes and non-irritating to the skin of rabbits. It was not a skin sensitizer in guinea pigs.

The end-use product, DuPont Acapela Fungicide, was of low oral, dermal and inhalation toxicity in rats. It was minimally irritating to the eyes and slightly irritating to the skin of rabbits. It was not a dermal sensitizer in guinea pigs.

After repeated dosing, the mucous membranes of the G.I. tract were the primary target in all species tested either via diet or gavage. Mice exhibited inflammation and erosion of the non-glandular stomach in females and hyperplasia of the duodenal and stomach glandular mucosa and dilatation of the mucosal glands in males following 18 months of dietary exposure. In the rat developmental toxicity study, there were increases in diarrhea and post-dosing salivation in treated animals. In the 2-year dietary toxicity study in rats, treated animals exhibited increased incidents of soft feces. The dog exhibited signs of G.I. tract irritation at the lowest doses in the database. In the 90-day dietary toxicity study in dogs, males and females exhibited fluid feces and females exhibited increased salivation at feeding. In the 1-year dietary toxicity study in dogs, males exhibited increased salivation and red sclera.

In general, concurrent with irritation of the G.I. tract in all repeat-dose test species, body weight, body weight gain and food consumption were decreased.

In the acute gavage neurotoxicity study in rats, animals treated with the lowest dose exhibited low arousal and reduced motor activity in males and a reduction in rearing in females. At higher doses, there was a reduction in food consumption, increases in stained fur and skin, diarrhea, palpebral closure, curled-up posture, low body temperature and high carriage. At the highest dose, there was increased mortality in the females, increased soiling of the fur and skin in both sexes, and increased red nasal discharge and uncoordinated gait and abnormal posture in females. In the dietary subchronic neurotoxicity rat study, body weights and body weight gains were decreased at the mid-dose in females and at the high dose in males. At the high dose, food consumption was decreased in males and females, grip strength was decreased in males and landing foot splay was increased in females.

In the mouse dietary oncogenicity study, there was no evidence of tumours. The doses tested did not reach the maximum tolerated dose (MTD) in females, but approached the limit dose and showed overt toxicity in males. In the combined chronic/oncogenicity study in rats, there was a treatment-related increase in interstitial cell testicular adenomas. The tumours occurred at the high dose and in the presence of decreased body weights and body weight gain and increased incidences of soft feces, effects that were seen at lower doses throughout the database.

This is a common tumour in the aging rat, there was no progression to carcinomas, no decrease in the latency period and the tumours occurred at doses that exceeded the MTD. As the genotoxicity battery was negative and the tumours occurred only at the highest dose tested in the presence of overt toxicity, the tumours were deemed to exhibit a non-genotoxic threshold response.

In the developmental toxicity studies in rats and rabbits, offspring exhibited increases in skeletal variations at the same doses causing maternal toxicity (decreased body weight and increased diarrhea and post-dosing salivation in rats and decreased body weight gains in rabbits). At lower levels, rabbit dams exhibited an increase in diarrhea, decreased feces, decreased food consumption and decreased gravid uterine weights. In rats, there was an increase in skeletal variations at the highest dose where dams exhibited increased diarrhea and post-dosing salivation. In one reproductive toxicity study in rats, offspring exhibited decreased body weights in the first and second generations at doses greater than or equal to doses causing decreased body weight and food consumption in adult animals. In the second reproductive toxicity study in rats, offspring exhibited decreased spleen weights at doses that did not cause parental toxicity and decreased thymus, thyroid and adrenal weights at doses that caused decreased body weights, food consumption and food efficiency in the adults. The toxicological significance of this change in spleen weight is unknown in the absence of any signs of immunotoxicity in the database. There were no effects on the reproductive parameters.

There were no adverse effects up to the limit dose in two 28-day dermal toxicity studies in rats. There were no treatment-related effects in either rats or mice in immunotoxicity studies.

An acute inhalation toxicity study was performed on a volatile soil metabolite that did not appear in the rat metabolism study, metabolite 26 (R413834). The study did not provide particle size information; however, treated animals exhibited signs of neurological toxicity similar to those seen in the acute neurotoxicity study in rats, but at doses that exceeded the limit dose. These clinical signs consisted of reduced reactivity, responsivity and reflexes and increased salivation, staining and lacrymation, as well as decreased body weight.

Results of the toxicology studies conducted on laboratory animals with picoxystrobin 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 picoxystrobin, and any additional information submitted by the applicant during the review process was considered. As of December 30, 2011, there were no health-related incident 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 *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, extensive data were available for picoxystrobin. The database contains the full complement of required studies including developmental toxicity studies in rats and rabbits and two reproductive toxicity studies 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 prenatal developmental toxicity studies. Minor developmental effects (increased incidence of skeletal variations) were observed in the rat and rabbit developmental toxicity studies; however, these effects occurred in the presence of maternal toxicity. In one of the 2-generation rat reproductive toxicity studies, offspring spleen weights were decreased in the absence of maternal toxicity; however, there was low concern as there is sufficient margin between this endpoint and the point of departure for the risk assessment. At higher doses, offspring body weights, thymus, thyroid and adrenal weights were decreased in the presence of decreased maternal body weights, body weight gain, food consumption and food efficiency. Though there were apparent effects on organs associated with the immune system in offspring, there were no histopathological changes in the offspring and no effects on the adult immune system organs or functionality. Overall, 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 Acute Reference Dose (ARfD)

General Population

To estimate acute dietary risk (1 day), the acute neurotoxicitystudy in rats with a LOAEL of 200 mg/kg bw was selected for risk assessment. At the LOAEL of 200 mg/kg bw, low arousal and reduced motor activity in males and a reduction in rearing in females were observed. These effects were the result of a single exposure and are therefore relevant to an acute risk assessment. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. An additional 3-fold uncertainty factor has been applied for the lack of a NOAEL in the acute neurotoxicity study. As discussed in the PCPA Hazard Characterization section, the PCPA factor was reduced to 1-fold. **The composite assessment factor (CAF) is 300.**

The ARfD is calculated according to the following formula:

$$\text{ARfD (gen. pop)} = \frac{\text{LOAEL}}{\text{CAF}} = \frac{200 \text{ mg/kg bw}}{300} = 0.67 \text{ mg/kg bw of picoxystrobin}$$

3.3 Acceptable Daily Intake (ADI)

To estimate dietary risk from repeated exposure, the 1-year dietary dog study with a NOAEL of 4.6 mg/kg bw/day was selected for risk assessment. At the LOAEL of 15.7 mg/kg bw/day, decreased body weight, body weight gain and food consumption were observed in males and females and increased salivation and red sclera were observed in males. 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.**

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{4.6 \text{ mg/kg bw/day}}{100} = 0.046 \text{ mg/kg bw/day of picoxystrobin}$$

The ADI provides a margin of greater than 1100 to the NOAEL at which testicular interstitial adenomas were observed in rats and 370 to reduced spleen weights in offspring in rats.

Cancer Assessment

Picoxystrobin showed evidence of oncogenicity in rats at levels that demonstrate overt toxicity. A threshold approach for risk assessment for testicular tumours in male rats was deemed appropriate. As discussed previously, the tumours occurred at doses that exceeded the MTD, were a common tumour in the aging rat and there was no progression to carcinomas or decrease in latency period. The dietary reference dose (i.e. the ADI), as well as the selected NOAELs and the target margins of exposure (MOE) for occupational and bystander exposure, provide a sufficient margin to these tumours.

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 two 28-day dermal toxicity studies were selected. The studies addressed the endpoints of concern in the rest of the database. There were no treatment-related effects at the NOAEL (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 8.5 mg/kg bw/day from the 90-day dietary dog toxicity study was selected. There were no repeat-dose inhalation studies submitted for this chemical. The NOAEL was based on decreased food consumption and an increase in fluid feces in both sexes, decreased body weights and body weight gains in males, and increased salivation at feeding in females at the LOAEL of 16.5/16.9 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.

3.4.1.1 Dermal Absorption

Studies designed to estimate the dermal penetration of picoxystrobin were submitted and have been reviewed. The studies were found to be acceptable for estimating dermal absorption, however, since a dermal toxicological endpoint was available, these studies were not used for estimating exposure to workers.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/Loader/Applicator Exposure and Risk Assessment

Individuals have potential for exposure to picoxystrobin during mixing, loading and application. Exposure to workers mixing, loading and applying DuPont Acapela Fungicide is expected to occur primarily by the dermal and inhalation routes. Farmers are expected to be exposed for short-term duration, and custom applicators are expected to be exposed for intermediate-term duration. Exposure estimates for picoxystrobin were derived for mixer/loader/applicators using groundboom equipment for the treatment of cereals, corn, dry legumes and soybeans. In addition, exposure estimates were derived for mixer/loader/applicators applying picoxystrobin using aerial equipment. The exposure estimates are based on mixers/loaders wearing a long-sleeved shirt, long pants, shoes, socks plus chemical-resistant gloves and applicators wearing a long-sleeved shirt, long pants and shoes plus socks.

As chemical-specific data for assessing human exposures during pesticide handling activities were not submitted, dermal and inhalation exposure estimates for workers were generated using the Pesticide Handlers Exposure Database (PHED), version 1.1.

Dermal exposure was estimated by coupling the unit exposure values with the amount of product handled per day. The dermal absorption was not used in the calculation of dermal exposure, since the short- to intermediate-term dermal endpoint is based on a dermal toxicity study. Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight.

Exposure estimates were compared to the toxicological endpoints (NOAEL) to obtain the margin of exposure (MOE); the target MOE is 100.

Table 1.1: Mixer/Loader/Applicator Dermal Exposure Estimates and MOEs

Exposure scenario	PPE Scenario	Area Treated per day (ha)[1]	Total Dermal Unit Exposure (µg/kg a.i. handled)	Rate (kg a.i./ha)	Dermal Exp. Estimates (mg a.i./ kg bw/day)[2]	Dermal MOE[3]
Famer (M/L/A)	Single layer plus gloves (M/L), single layer (A)	107	84.12	0.22	0.02829	35,350
Custom (M/L)	Single layer plus gloves	360	51.14	0.22	0.05786	17,290
Custom (A)	Single layer	360	32.98	0.22	0.03731	26,800
Aerial (M/L)	Single layer plus gloves	400	51.14	0.22	0.06429	15,550
Aerial (A)	Single layer	400	9.66	0.22	0.0121	82,350

M/L = mixer/loader, A = applicator, M/L/A = Mixer/loader/applicator
[1] Default Area Treated Per Day values
[2] Daily exposure = (PHED unit exposure x ATPD x Rate) / (70 kg bw x 1000 µg/mg)
[3] Based on dermal NOAEL= 1000 mg/kg bw/day; target MOE = 100

Table 1.2: Mixer/Loader/Applicator Inhalation Exposure Estimates and MOEs

Exposure scenario	PPE Scenario	Area Treated per day (ha)[1]	Total Inhalation Unit Exposure (µg/kg a.i. handled)	Max Rate (kg a.i./ha)	Inhalation Exp. Estimates (mg a.i./ kg bw/day)[2]	Inhalation MOE[3]
Famer (M/L/A)	Single layer plus gloves (M/L), single layer (A)	107	2.56	0.22	8.61×10^{-4}	9,870
Custom (M/L)	Single layer plus gloves	360	1.6	0.22	1.81×10^{-3}	4,700
Custom (A)	Single layer	360	0.96	0.22	1.09×10^{-3}	7,830
Aerial (M/L)	Single layer plus gloves	400	1.60	0.22	2.01×10^{-3}	4,230
Aerial (A)	Single layer	400	0.07	0.22	8.8×10^{-5}	96,590

M/L = mixer/loader, A = applicator, M/L/A = Mixer/loader/applicator

[1] Default Area Treated Per Day values

[2] Daily exposure = (PHED unit exposure x ATPD x Rate) / (70 kg bw x 1000 µg/mg)

[3] **Based on oral NOAEL= 8.5 mg/kg bw/day; target MOE = 100**

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers entering areas treated with picoxystrobin while performing activities such as scouting, irrigating, detasseling, hand harvesting, and thinning. The duration of exposure is considered to be short- to intermediate-term for all uses. The primary route of exposure for workers re-entering treated areas would be through the dermal route. Inhalation exposure is not considered to be a significant route of exposure for people entering treated areas compared to the dermal route, since picoxystrobin is relatively non-volatile (1.4×10^{-8} kPa at 25°C) and as such, a risk assessment was not required.

Dermal exposure to workers entering treated areas is estimated by coupling chemical specific dislodgeable foliar residue values with activity-specific transfer coefficients (TCs). Activity TCs are based on EPA Policy 3.1 and Agricultural Re-entry Task Force (ARTF) data.

Chemical-specific dislodgeable foliar residue (DFR) data were submitted. This study was designed to determine the dissipation of DFR of picoxystrobin after application to the foliage of soybeans. The field trials were conducted in three NAFTA Growing Zones (1, 2, and 5). The sites were Germansville, PA, Seven Springs, NC, and Conklin, MI. DuPont Acapela Fungicide is a suspension concentrate (SC) containing 250 g of active ingredient per litre of formulation which is coded picoxystrobin 250SC. The test product was applied once to each of the three sites at a target application rate of 220 g a.i. /hectare (labelled maximum rate) in approximately 145 to 200 litres of spray solution per sprayed hectare. Surfactants/adjuvants were included in the spray mixture. Treatments were applied using either handheld or tractor mounted boom sprayer equipment. Surfactants/adjuvants were added to the spray tank mixture. Samples were collected approximately two days to one hour before and approximately two hours after the application,

and 1, 2, 5, 7, 10, 14, and 21 days after application. The average field fortification recoveries were >90%.

At the Germansville, PA site, the highest average picoxystrobin residue was 0.221 μg/cm^2, which occurred within 2 hours after application. The residues declined to <LOQ values within 7 days of treatment (7 DAT). At the Seven Springs, NC site, the highest average residue was 0.347 μg/cm^2 which occurred 2 DAT. By 10 DAT, residues were <LOQ. At the Conklin, MI site, the highest average residue was 0.208 μg/cm^2 at 2 DAT. DFRs declined to levels <LOQ by 10 DAT (see Appendix I, Table 4).

First-order dissipation kinetics was assumed to determine the half-life of picoxystrobin residues on soybean leaves and a linear regression analysis was performed. Estimated half-life values were 1.1 days (R^2 = 0.949) at Germansville, PA site, 1.7 days (R^2 = 0.740) at the Seven Springs, NC site and 2.0 days (R^2 = 0.842) at the Conklin, MI site (see Appendix I, Table 4).

Soybeans are considered to be a good surrogate crop since the leaf type, like all the proposed crops, is smooth and groundboom was used for application (which is the proposed method for application and should also be representative of aerial application). Based on the climate zones for each replicate, temperature and the total rainfall, the Conklin, MI data are considered to be the most relevant to the soybean growing regions in Canada. The Conklin, MI data have a better R^2 value than the Seven Springs, NC data and neither site had any rainfall during the first few days after application (no rainfall events during the day of application or on days 1 and 2 after application). The Germansville, PA site had higher R^2 value but also had rainfall on days 0, 1 and 2 after application. The Conklin, MI data are considered to be the most conservative for dissipation while also having the lowest predicted day 0 residues. Therefore, for the purpose of this application the day 0 residues will be calculated using 9.3% of the application rate with a dissipation of 28.7% per day.

Exposure estimates were compared to the toxicological endpoint to obtain the MOE; the target MOE is 100. The REI of 12 hours and pre-harvest intervals (PHIs) are adequate to protect re-entry workers.

Table 2 Postapplication Margin of Exposure on Cereals, Corn, Dry Legumes and Soybeans

Crops	Max # of applications	Max Rate (g a.i./ha)	Postapplication activity	Predicted DFR after max number of applications ($\mu g/cm^2$)[1]	TC (cm^2/hr)[2]	Exposure after max number of applications (mg/kg bw/day)[3]	Calculated MOE[4]
Cereals	3	220	Scouting, (irrigating) in full foliage	0.2256	1,500	0.0387	25,860
Corn (sweet, field and seed)	5	200	Detasseling seed corn	0.2052	17,000	0.0352	2,510
Dry legumes, soybeans	3*	220	Scouting and irrigating in full foliage	0.2256	1,500	0.0387	25,860

* Only 2 applications for dry legumes and 3 for soybeans.
[1] Calculated based on soybean study DFR values (9.3% DFR on Day 0 after a single application, and 28.7% dissipation per day).
[2] Transfer coefficients from EPA Policy 3.1 and ARTF Database
[3] Exposure = (Peak DFR × TC × 8 hr/day) / (70 kg bw × 1000 µg/mg)
[4] Based on NOAEL = 1000 mg/kg bw/day, target MOE = 100

There is also the potential for workers entering treated areas to be exposed to Compound 26. Compound 26 is a transformation product of picoxystrobin formed in soil, which has been shown to be acutely hazardous via the inhalation route. The applicant submitted a preliminary review of an air monitoring study for Compound 26. In the study, two applications of picoxystrobin (250 g a.i./ha) were made to winter wheat at a 14-day spray interval. Monitoring occurred following the first application until 62 days after harvest of the wheat. During this time, air samples were collected once per week, each sampling occasion covering a 24-hour period. Air monitoring revealed that concentrations of Compound 26 in the air over the treated field were below the level of detection (LOD) in all instances (<0.1 ng/L).

These results confirm that a large one-time exposure to Compound 26 is not realistic; therefore, the concentrations used in the 4-hour acute laboratory inhalation study are not expected to occur in the field. For these reasons, a postapplication acute inhalation risk assessment for re-entry workers to Compound 26 is not required.

3.4.3.3 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. However, a statement is required that limits application 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 picoxystrobin in plant and livestock commodities. The LC-MS/MS enforcement analytical method# Du-Pont-29312 is valid for the quantitation of picoxystrobin residues in plant matrices. The LC-MS/MS enforcement analytical method# Du-Pont-25997 (Revision No. 1) is valid for the quantitation of picoxystrobin residues in livestock matrices. The residues of picoxystrobin are stable in plant commodities when stored frozen (< -18°C) for up to 12 months and in cereal matrices for up to 22 months. Processing factors are determined to be 2.0x in wheat bran, 3.2x in wheat germ, 6.8x in refined corn oil, and 1.3x in soybean oil. The anticipated picoxystrobin residues are <0.01 in eggs, milk, fat, meat, meat by-products of cattle, goats, hogs, horses, poultry and sheep. Supervised residue trials conducted throughout Canada and the United States using end-use products containing picoxystrobin at the proposed rates in/on corn (field and sweet), wheat, barley, soybean, dried pea and bean, and canola are sufficient to support the proposed maximum residue limits.

3.5.2 Exposure from Drinking Water

3.5.2.1 Concentrations in Drinking Water

Estimated environmental concentrations (EECs) of picoxystrobin 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 picoxystrobin 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 picoxystrobin 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.

There are several transformation products of picoxystrobin, and three products were included in the drinking water modelling. These transformation products are Compound 2, Compound 3 and Compound 8. In the current assessment, a combined residue of the parent and the above three transformation products was modelled for drinking water. Thus environmental half-lives in soil and water were calculated for the combined residues of parent and three transformation products.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EEC estimates are expected to allow for future use expansion into other crops at this application rate. Table 3.5.2-1 lists the application information and main environmental fate characteristics used in the simulations. Nine initial application dates (five for surface water and four for

groundwater) between June and July were modelled. The model was run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Table 3.5.2-2 below.

Table 3.5.2-1. Major groundwater and surface water model inputs for Level 1 assessment of picoxystrobin

Type of Input	Parameter	Value
Application Information	Crops to be treated	corn (sweet, field, seed, popcorn), cereals, dry legumes and soybeans
	Maximum allowable application rate per year (g a.i./ha)	875 for sweet corn 437.5 for dry legumes
	Maximum rate each application (g a.i./ha)	200 for sweet corn 220 for dry legumes
	Maximum number of applications per year	not specified
	Minimum interval between applications (days)	sweet corn: 7 but without 2 sequential applications before switching to a fungicide with a different mode of action dry legumes: 14 (although the label states 7 days, no more than 1 application is allowed before switching to a fungicide with a different mode of action, thus the interval for modelling was 14 days)
	Method of application	aerial and ground
Environmental Fate Characteristics	Hydrolysis half-life at pH 7 (days)	stable
	Photolysis half-life in water (days)	25
	Adsorption K_{OC} (mL/g)	837 (20^{th} percentile of six K_{OC} values for "picoxystrobin")
	Aerobic soil biotransformation half-life (days)	33.28 for parent (80^{th} percentile of four half-life values) 61.16 for the combines residues (80^{th} percentile of 4 half-life values)
	Aerobic aquatic biotransformation half-life (days)	57.3 for parent (longest of two half-lives) 518 for the combined residues (longest of two half-lives)
	Anaerobic aquatic biotransformation half-life (days)	54.2 for parent (one half-life available) 2970 for the combined residues (one half-life available)

Table 3.5.2-2. Level 1 estimated environmental concentrations of the combined residues of picoxystrobin (parent + Compounds 2, 3 and 8) in potential drinking water sources (rate of 200+ 200+ 200+140+135 g a.i./ha for use on sweet corn)

Compound	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)			
			Reservoir		Dugout	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[3]	Yearly[4]
Combined residues of picoxystrobin and Compounds 2, 3 and 8	0.22	0.22	27	8.1	81	73

[1] 90th percentile of daily average concentrations
[2] 90th percentile of yearly average concentrations
[3] 90th percentile of yearly peak concentrations
[4] 90th percentile of yearly average concentrations

3.5.3 Dietary Risk Assessment

Acute and 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.

3.5.3.1 Chronic Dietary Exposure Results and Characterization

For the chronic dietary exposure assessment, MRL-level residues were used for all domestic and imported crops and livestock commodities. It was assumed that 100% of the crops were treated. The basic chronic dietary exposure from all supported picoxystrobin food uses (alone) for the general population, including infants and children, and all representative population subgroups is ≤0.7% of the acceptable daily intake. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to picoxystrobin from food and water is 1.0% (0.000483 mg/kg bw/day) of the ADI for the general population. The highest exposure and risk estimate is for children of 1-2 yrs old at 2.4% (0.001108 mg/kg bw/day) of the ADI.

3.5.3.2 Acute Dietary Exposure Results and Characterization

The basic acute dietary exposure (food alone) from all proposed picoxystrobin food uses is estimated to be 0.13% (0.000853 mg/kg bw/day) of the ARfD for the general population (95th percentile, deterministic). Aggregate exposure from food and water is considered acceptable at 0.29% of the ARfD (0.001973 mg/kg bw/day) for the general population (95th percentile, deterministic). The highest exposure and risk estimate is for all infants (<1 year old) at 0.87% (0.005853 mg/kg bw/day) of the ARfD (95th percentile, deterministic).

3.5.4 Aggregate Exposure and Risk

The aggregate risk for picoxystrobin consists of exposure from food and drinking water sources only. Aggregate risks were calculated based on acute and chronic endpoints.

3.5.5 Maximum Residue Limits

Table 3.5.5-1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Barley bran	0.5
Barley	0.3
Wheat germ	0.09
Crop Subgroup 20A (Rapeseed Subgroup)	0.08
Corn oil	0.07
Crop Subgroup 6C (Dried Shelled Pea and Bean, except soybean)	0.06
Wheat bran	0.06
Dry soybeans	0.05
Crop Group 15 (Cereal Grains, except barley and rice)	0.04
Eggs	0.01
Fat, meat and meat by-products of cattle, goats, hogs, horses, poultry, and sheep	0.01
Milk	0.01

For additional information on Maximum Residue Limits (MRL) 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 acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 5 and 6.

4.0 Impact on the Environment

Fate and Behaviour in the Environment

Based on its physical-chemical properties, picoxystrobin has low solubility in water, is not likely to volatilize from moist soil or water surfaces under field conditions, has a limited potential to photodegrade in the environment, and could potentially bioaccumulate in aquatic organisms.

Environmental fate data for picoxystrobin and its transformation products are summarized in Appendix I, Table 8. A summary of the identity of transformation products of picoxystrobin formed in the environment is presented in Appendix I, Table 9. The maximum formation rate (as a percentage of the applied radioactivity) and time of maximum occurrence of transformation products in each study is included in Appendix I, Table 10.

Once picoxystrobin enters the terrestrial environment, it is expected to adsorb to soil. Laboratory studies on adsorption/desorption indicate that picoxystrobin has low mobility in soil. Picoxystrobin is slightly persistent in aerobic soil, where it undergoes microbial biotransformation. The major transformation products Compound 2 and Compound 3 are moderately persistent based on laboratory biotransformation studies. Compound 26 is volatile; however, evidence shows that Compound 26 may undergo some degradation if contained in the soil. Phototransformation is not expected to be an important route of degradation of picoxystrobin on soil. In terrestrial field studies, picoxystrobin was non-persistent to slightly persistent, Compound 2 was moderately persistent, and Compounds 3 and 8 were non-persistent to persistent. No significant carry over of picoxystrobin or transformation products to the following growing season is expected. There was little evidence of vertical movement in the soil except at one field site where precipation levels were very high, and Compound 8 was detected at depths of 50 – 70 cm. Water modelling of multi-year applications of picoxystrobin at the maximum seasonal rate indicate that levels of picoxystrobin and Compounds 2, 3 and 8 in groundwater are expected to be very low. Air sampling during field dissipation studies indicated that levels of Compound 26 after application of picoxystrobin were below the limit of quantification of 0.1 ng/L. There is some uncertainty as to the persistence and potential for long-range transport of the volatile transformation product, Compound 26, in the atmosphere.

Picoxystrobin can enter the aquatic environment through spray drift and runoff, likely bound to soil particles. Once in the water, picoxystrobin is not expected to hydrolyse. In water/sediment systems, approximately half of applied picoxystrobin will partition to sediments within a few days. Microbial degradation is the most important route of dissipation for picoxystrobin in the aquatic environment. Picoxystrobin is moderately persistent in both aerobic and anaerobic water/sediment systems. Major transformation products Compounds 2, 3, 7 and 8 were detected in the water and sediment layers of aquatic systems. They generally accumulated in both the water and sediment phases in laboratory studies. Phototransformation can contribute to the degradation of picoxystrobin but this process is not expected to be an important route of degradation of picoxystrobin in the environment.
Compounds 4 and 12 were major products of phototransformation. However, these transformation products are not expected to be formed in important quantities in the environment. Picoxystrobin does not appreciably bioconcentrate in fish.

4.1 Environmental Risk Characterization

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

Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

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

4.1.1 Risks to Terrestrial Organisms

A risk assessment of picoxystrobin and the transformation products Compound 2, Compound 3 and Compound 8 was undertaken for terrestrial organisms based on available toxicity data for each of the compounds to earthworms (acute and chronic exposure as well as field studies), bees (acute oral and acute contact exposure), non-target beneficial arthropods (acute contact laboratory studies, aged residue and semi-field studies), birds (acute oral, dietary and reproduction), mammals (acute oral and reproduction) and terrestrial plants (effects on seedling emergence and vegetative vigour). A summary of terrestrial toxicity data for picoxystrobin and its transformation products is presented in Table 11 (Appendix I) and the accompanying screening level risk assessment is in Table 12 (Appendix I) for terrestrial organisms other than birds and mammals, and Table 13 (Appendix I) for birds and mammals.

Earthworms: Picoxystrobin was acutely toxic to earthworms. The transformation products Compounds 2, 3 and 8 were much less toxic than the parent to earthworms. Earthworm reproduction was adversely affected by chronic exposure to picoxystrobin. The risk to earthworms resulting from acute and chronic exposure to picoxystrobin does not exceed the level of concern based on results of laboratory studies. The risk to earthworms from acute exposure to transformation products Compounds 2, 3 and 8 does not exceed the level of concern (Appendix I, Table 12). Risk was assessed based on EECs for the highest use rate scenario of DuPont Acapela Fungicide on sweet corn. As no risk was indicated for the use pattern on corn, risk quotients were not calculated for the use on dry legumes, which has a lower seasonal rate of application.

Based on results of laboratory studies, there is no indication that risks to earthworms are expected from exposure to picoxystrobin. However, field studies indicate that application of picoxystrobin at rates representative of Canadian uses could result in earthworm mortalities of approximately 50% within a few days of application if irrigation or precipitation occurs following application. At all but one field site, earthworm populations recovered from the initial effects of picoxystrobin within one year of application. A label statement to inform the users of the toxicity of picoxystrobin to earthworms is required on the product label.

Bees (pollinators): Acute oral and contact exposure to picoxystrobin and a 250 g a.i./L Soluble Concentrate formulation 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 level of concern, indicating picoxystrobin is not expected to pose a risk to pollinators (Appendix I, Table 12).

Beneficial arthropods: The toxicity of picoxystrobin was determined for a glass plate (screening level) exposure to the predatory mite (*Typholodromus pyri*), a semi-field exposure to the green lacewing (*Chrysoperlea carnea*) as well as a leaf substrate (extended laboratory) exposure and an aged residue exposure to the parasitic wasp (*Aphidius rhopalosiphi*). The risk to predatory and parasitic arthropods was assessed using maximum cumulative in-field and off-field EECs on plant surfaces, calculated from a direct spray on a field.

Based on results of a screening level glass plate study with the predatory mite, *Typhlodromus pyri*, exposure to picoxystrobin at rates of 250 and 500 g a.i./ha resulted in mortalities of approximately 50% after 7 days. The risk quotients from in-field and off-field exposures to picoxystrobin may exceed the level of concern for uses on sweet corn and dry legumes. Extended laboratory studies with *Typhlodromus pyri* were not submitted, and thus the risk to this organism could not be further characterized. There is uncertainty related to the potential for effects on *Typhlodromus pyri* as a result of use of picoxystrobin.

A semi-field study conducted with the green lacewing, *Chrysoperla carnea*, showed no significant effects on mortality and fecundity after one or two applications of picoxystrobin at 250 g a.i./ha (Appendix I, Table 12). However, the proposed uses of picoxystrobin in Canada could result in different and potentially higher environmental exposures than were tested in the study. There is uncertainty as to whether effects on the green lacewing, *Chrysoperla carnea*, are expected as a result of picoxystrobin use.

Complete mortality (100%) of the parasitic wasp, *Aphidius rhopalosiphi*, was observed after 48 hours of exposure to barley seedlings treated with picoxystrobin at rates of 250 g a.i./ha and 500 g a.i./ha. The risk quotients from in-field exposures to picoxystrobin exceed the level of concern; those from off-field exposures may exceed the level of concern. The risk to the parasitic wasp, *Aphidius rhopalosiphi*, was further characterized using results from a study involving exposure to aged residues of picoxystrobin. Exposure of *Aphidius rhopalosiphi* to fresh residues (Day 0) of picoxystrobin applied one or two times at 250 g a.i./ha resulted in 65.2% and 74.4% mortality, respectively.

Using a Day 0 LR_{50} (fresh residues) of <250 g a.i./ha, the risk quotients exceeded the level of concern for both uses on sweet corn and dry legumes (Appendix I, Table 12). Picoxystrobin can pose a risk to the parasitic wasp, *Aphidius rhopalosiphi*.

Based on the overall risk assesment for beneficial arthropods, a statement is required on the label for the end-use product, DuPont Acapela Fungicide, to inform users of the potential risks to predatory and parasitic arthropods which are used in Integrated Pest Management.

Birds: Picoxystrobin was not toxic to bobwhite quail (*Colinus virginianus*) on an acute oral basis, with no treatment-related mortalities occurring. Regurgitation occurred at the three highest doses tested in an acute oral study on the zebra finch (*Taeniopygia guttata*). An initial screening assessment as done for this species using a conservative acute oral LD_{50} set at a dose at which no regurgitation was observed, no mortalities occurred and no clinical signs of toxicity were noted. During short-term dietary exposure to bobwhite quail and mallard duck, no treatment-related mortality occurred; however, mallard ducks experienced a reduction in weight gain at the two highest concentrations tested. During 20- and 21-week dietary exposure studies, no treatment-related adverse effects on overall survival or reproductive performance of either bobwhite quail or mallard ducks were observed (Appendix I, Table 11). The risk quotients for acute and reproductive exposure to birds do not exceed the level of concern for small, medium or large birds (Appendix I, Table 13). Risk was assessed based on EECs for the highest proposed use rate scenario of DuPont Acapela Fungicide on sweet corn. As no risk was indicated for this use pattern, risk quotients were not calculated for the proposed use on dry legumes, which has a lower seasonal rate of application.

Mammals: The laboratory toxicity of picoxystrobin, a 250 g/L Soluble Concentrate formulation, and the transformation product Compound 26 to rats was used to assess risk to small terrestrial mammals. Picoxystrobin and the 250 g a.i./L formulation were not acutely toxic to rats (Appendix I, Table 11). Reproductive performance in rats was not affected by exposure to picoxystrobin. A screening level risk assessment for three size classes of small mammals based on a conservative assumption of vegetation and insect food sources did not identify a concern for acute mortality or reproductive risks for picoxystrobin exposure from use on sweet corn (Appendix I, Table 13). Two mortalities were observed in females at the highest dose tested in an acute inhalation study with Compound 26 (Appendix I, Table 11). A quantitative assessment of the inhalation risk of the volatile transformation product, Compound 26, to mammals has not been done. Picoxystrobin is not volatile, and Compound 26 was a transformation product only formed in soil. This would likely result in a slow release of Compound 26 over time and not a large one-time exposure as would be the case with fumigants, or with volatile active ingredients applied to soil. The concentrations used in the 4-hour acute laboratory inhalation study are not expected to occur in the field. A field study where two applications of picoxystrobin at 250 g a.i./ha were made to winter wheat at a 14-day interval revealed that concentrations of Compound 26 in the air over the treated field were below the limit of quantification (0.1 ng/L). Monitoring occurred following the first application until 62 days after harvest of the wheat. During this time, air samples were collected once per week, each sampling occasion covering a 24-hour period.

These results confirm that a large one-time exposure to Compound 26 is not realistic. For the reasons outline above, a risk to small mammals from acute exposure via inhalation of Compound 26 is not expected.

Non-target plants: The toxicity of a 250 g a.i./L Soluble Concentrate formulation of picoxystrobin to non-target plants was determined through vegetative vigour and seedling emergence assays using standard crop species. No significant adverse effects (i.e., >25% effect) were observed in any plant species in either assay (Appendix I, Table 11). The EC_{25} is therefore >500 g a.i./ha. The screening level risk assessment for the picoxystrobin formulation determined that the level of concern for the use on sweet corn may be slightly exceeded, as the risk quotient was <1.2 for seedling emergence (Appendix I, Table12). It is not certain whether the level of concern has been exceeded, as the risk quotient is based on an endpoint greater than the highest rate tested but this rate is less than the expected environmental concentrations for the proposed Canadian use pattern. The level of concern was not exceeded for the proposed use on dry legumes. Picoxystrobin may pose a risk to non-target terrestrial plants at some of the proposed Canadian use rates. Spray buffer zones are required for some proposed uses of picoxystrobin, to mitigate potential effects of spray drift to non-target terrestrial plants.

4.1.2 Risks to Aquatic Organisms

Aquatic organisms can be exposed to picoxystrobin 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 sweet corn and dry legumes were used as the exposure estimates. A risk assessment of picoxystrobin, a 250 g a.i./L Soluble Concentrate formulation, and the five transformation products Compounds 2, 3, 7, 8 and 26 was undertaken for freshwater and marine aquatic organisms based on available toxicity data for each of the compounds to algae (acute), aquatic plants (acute), invertebrates (acute and chronic), fish (acute and chronic) and amphibians (using fish as surrogate data). A summary of aquatic toxicity data for picoxystrobin, a 250 g a.i./L Soluble Concentrate formulation and transformation products is presented in Table 14 (Appendix I).

For acute toxicity studies, uncertainty factors of 1/2 and 1/10 the EC_{50} (LC_{50}) are typically used in modifying the toxicity values for aquatic plants and invertebrates, and fish species, respectively when calculating risk quotients (RQs). No uncertainty factors are applied to chronic NOEC endpoints. For picoxystrobin, multiple acute toxicity endpoints were available for freshwater invertebrates and freshwater fish. The program ETX 2.0 was used to generate species sensitivity distributions (SSDs) for freshwater invertebrates and freshwater fish based on normally distributed toxicity data. The hazardous concentration to 5% of the species (HC_5) was then calculated for both freshwater invertebrates and freshwater fish from their respective SSDs. The HC_5 values were used to calculate the risk quotients for these groups of taxa instead of the most sensitive species tested. This provides a more scientific endpoint, which uses all of the data. No uncertainty factors are applied to the HC_5 when calculating risk quotients. For groups where the level of concern (LOC) is exceeded (i.e., RQ $\geq$1), a refined Tier 1 assessment is conducted to determine risk resulting from spray drift and runoff separately. Risk quotients for picoxystrobin were calculated for uses on sweet corn and dry legumes, which have the highest and lowest

proposed seasonal application rates, respectively. The calculated risk quotients for picoxystrobin are summarized in Tables 15 (screening level), 16 (Tier 1 – spray drift only) and 17 (Tier 1 – runoff only) in Appendix I. For transformation products, risk was assessed based on EECs for the highest proposed use rate scenario of DuPont Acapela Fungicide on sweet corn. The screening level risk quotients for transformation products are summarized in Table 18 (Appendix I). As no risk was indicated for this proposed use pattern, risk quotients were not calculated for the proposed use on dry legumes, which has a lower proposed seasonal rate of application.

Freshwater algae and plants: Of the two algal and one plant species tested, picoxystrobin was toxic to green algae (*Selenastrum capricornutum*). Transformation products Compounds 2, 3, 7, 8 and 26 were much less toxic than the parent to green algae (Appendix I, Table 14). The screening level risk quotient for green algae exposed to picoxystrobin exceeded the level of concern for proposed uses on both sweet corn and dry legumes (risk quotients > 1; Appendix I, Table 15). Refined risk quotients based on spray drift of picoxystrobin slightly exceeded the level of concern for aerial application to sweet corn (risk quotient = 1.2), but not for field sprayer application; the level of concern was not exceeded for aerial and field sprayer application to dry legumes (Appendix I, Table 16). There is a potential risk to freshwater algae from some picoxystrobin proposed uses. Green algae are not expected to be at risk from picoxystrobin runoff inputs (Appendix I, Table 17). Screening level risk quotients for green algae exposed to transformation products did not exceed the level of concern. For the freshwater plant, duckweed, the screening level risk quotient for exposure to picoxystrobin for proposed uses on sweet corn or dry legumes did not exceed the level of concern (Appendix I, Table 15).

Freshwater invertebrates: Acute exposure to picoxystrobin resulted in significant mortality in several species of aquatic invertebrates. Transformation products were much less acutely toxic than the parent to *Daphnia magna*. Chronic exposure to picoxystrobin resulted in reduced reproduction of *Daphnia magna* and significant reduction in emergence rate of the freshwater midge, *Chironomus riparius* (Appendix I, Table 14). The screening level risk quotients for acute and chronic exposure of freshwater invertebrates to picoxystrobin exceeded the level of concern for the proposed use on sweet corn and on dry legumes (Appendix I, Table 15). The refined risk quotients based on spray drift of picoxystrobin slightly exceeded the level of concern for: acute exposure of freshwater invertebrates from aerial application to sweet corn; chronic exposure of *Daphnia magna* from aerial application to sweet corn and dry legumes; and chronic exposure of the freshwater midge from aerial application to sweet corn (Appendix I, Table 16). Thus, there is a potential risk to freshwater invertebrates exposed to picoxystrobin through spray drift from aerial application. Refined risk quotients based on runoff inputs did not exceed the level of concern for any freshwater invertebrate species, indicating that these organisms are not expected to be at risk from picoxystrobin runoff into water bodies (Appendix I, Table 17). Screening level risk quotients for picoxystrobin transformation products did not exceed the level of concern for acute exposure to *Daphnia magna* (Appendix I, Table 15).

Freshwater fish and amphibians: Acute exposure to picoxystrobin resulted in significant mortality to rainbow trout, common carp, bluegill sunfish, three-spined stickleback and fathead minnow. The acute risk of picoxystrobin to fish was assessed using the HC_5 based on effects

endpoints from toxicity studies with these five fish species. The chronic risk of picoxystrobin was assessed based on a 28-day toxicity study with the rainbow trout and an early life stage toxicity study with the fathead minnow. The acute risks for transformation products Compounds 2, 3, 7, 8 and 26 were assessed using toxicity studies with either the fathead minnow or the rainbow trout. Picoxystrobin was acutely toxic to freshwater fish, while the transformation products Compounds 2, 3, 7, 8 and 26 were not toxic. Exposure to picoxystrobin for 28 days resulted in reduced survival of rainbow trout, while exposure to picoxystrobin to early life stages of fathead minnow resulted in reductions in embryo hatching success, larval survival and larval growth (Appendix I, Table 14).

The screening level risk quotients for acute, chronic and early life stage exposures of freshwater fish to picoxystrobin exceeded the level of concern for both uses on sweet corn and dry legumes (Appendix I, Table 15). Refined risk quotients based on spray drift of picoxystrobin slightly exceeded the level of concern for a 28-day exposure of rainbow trout from aerial application to sweet corn and dry legumes (Appendix I, Table 16). Thus, there is a potential risk to freshwater fish exposed to picoxystrobin through spray drift from aerial application. Refined risk quotients based on runoff inputs did not exceed the level of concern for acute, chronic or early life stage exposure to freshwater fish, indicating that these organisms are not expected to be at risk from picoxystrobin runoff into water bodies (Appendix I, Table 17). The transformation products Compounds 2, 3, 7, 8 and 26 are not an acute risk to fish based on the screening level risk quotients (Appendix I, Table 15).

The risk for amphibians was characterized at the screening level by comparing EECs in 15 cm water depth with fish toxicity endpoints as surrogates for aquatic life-stages of amphibians. Acute risks were assessed for exposure to picoxystrobin and the transformation products Compounds 2, 3, 7, 8 and 26; chronic risk was assessed for picoxystrobin. The screening level risk quotients for amphibians exceeded the level of concern for the proposed uses on sweet corn and dry legumes (Appendix I, Table 15). Refined risk quotients based on spray drift of picoxystrobin exceeded the level of concern for acute and early life stage exposures from aerial application to sweet corn and dry legumes, and for a chronic (28-day) exposure from aerial and field sprayer application to sweet corn and dry legumes (Appendix I, Table 16). Thus, there is a potential risk to amphibians from exposure to picoxystrobin through spray drift. Refined risk quotients based on runoff inputs did not exceed the level of concern indicating that a risk to amphibians is not expected from picoxystrobin runoff into water bodies (Appendix I, Table 17). The transformation products Compounds 2, 3, 7, 8 and 26 are not an acute risk to amphibians based on the screening level risk quotients (Appendix I, Table 15).

Marine/estuarine species: Picoxystrobin was acutely toxic to the saltwater diatom (*Skeletonema costatum*), Eastern oyster (*Crassostrea virginica*), mysid shrimp (*Americamysis bahia*), and the sheepshead minnow (*Cyprinodon variegatus*). Exposure to picoxystrobin for 29 days resulted in reduced reproduction of mysid shrimp, while exposure to picoxystrobin to early life stages of sheepshead minnow affected larval growth (Appendix I, Table 14). For uses of picoxystrobin on sweet corn and dry legumes, the screening level risk quotients based on acute, chronic and/or early life stage exposures of marine/estuarine invertebrates, fish and algae exceeded the level of concern (Appendix I, Table 15). Refined risk quotients based on spray drift of picoxystrobin

exceeded the level of concern for mysid shrimp (aerial and field sprayer application to sweet corn, aerial application to dry legumes), Eastern oyster (aerial and field sprayer application to sweet corn and dry legumes) and saltwater diatom (aerial and field sprayer application to sweet corn and dry legumes), but not for fish (Appendix I, Table 16). Thus, there is a potential risk to marine/estuarine invertebrates, and algae exposed to picoxystrobin through spray drift from aerial and field sprayer application. Refined risk quotients based on runoff inputs did not exceed the level of concern indicating that a risk to marine/estuarine organisms is not expected from picoxystrobin runoff (Appendix I, Table 17).

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

Uses on the following crops and diseases were proposed: control of leaf rust, septoria leaf blotch, powdery mildew, and tan spot on cereals; control of northern corn leaf blight on corn; control of Asian soybean rust, brown spot, frogeye leafspot, and sclerotinia stem rot on soybeans; control of mycosphaerella blight, Asian soybean rust, and white mould on dry legumes. Aerial application was also proposed on all crops.

A total of 53 efficacy trials were submitted to support 12 use claims. The review focused on trials with moderate to high disease pressure. Efficacy data from 14 trials were not considered as disease pressure was too low to determine efficacy with confidence.

Twenty-seven trials conducted in Canada and the US between 2007 and 2009 were reviewed to support claims on cereal crops. The trials demonstrated that application of DuPont Acapela Fungicide at rates of 0.44 – 0.88 L/ha (110 – 220 g a.i./ha) controlled tan spot, septoria leaf blotch, leaf rust, and powdery mildew on cereals.

Three trials conducted in Canada and Italy in 2009 were reviewed to support the claim of control of northern corn leaf blight on corn at rates of 0.44 – 0.88 L/ha (110 – 220 g a.i./ha). Italian trials were accepted for review due to similarities in climate compared to Canada and because the environment was conducive to pest development. The submitted evidence demonstrated control of northern corn leaf blight on corn when DuPont Acapela Fungicide was applied as proposed.

Eighteen trials conducted in Canada, the US and Brazil were reviewed to support claims on soybean. Data from Brazil was accepted to support the claim of control of Asian soybean rust as introduction of this disease to Canadian agricultural regions is undesirable. The trials demonstrated that DuPont Acapela Fungicide controls Asian soybean rust, brown spot and frogeye leafspot and suppresses sclerotinia stem rot on soybean when applied at 0.44 – 0.88 L/ha (110 – 200 g a.i./ha).

Eleven trials conducted in Canada and the US in 2008 and 2009 were reviewed to support claims on dry legumes. The trials demonstrated control of mycosphaerella blight on pea and suppression

of white mould on the dry legume crop group when DuPont Acapela Fungicide is applied at 0.6 – 0.88 L/ha (150 – 220 g a.i./ha). The claim of control of Asian soybean rust was extrapolated to the dry legume crop group from soybean data.

All 12 use claims were supported based on the submitted efficacy data. Four claims were supported with the condition that confirmatory data be submitted. Confirmatory data have been requested when efficacy was inconsistent in trials. A total of seven trials have been requested to confirm the level of efficacy; however, value data, including history of use information and benefits analysis, or scientific rationales will be considered in lieu of efficacy trials. Aerial application was supported on all crops.

5.2 Economics

No market analysis was done for this application.

5.3 Sustainability

5.3.1 Survey of Alternatives

A number of fungicides are registered on the labelled crops to control or suppress plant diseases registered on the DuPont Acapela Fungicide label. Refer to Appendix I, Table 20 for further information on alternative products.

5.3.2 Compatibility with Current Management Practices Including Integrated Pest Management

The use of integrated pest management (IPM) plans for the labelled crops would typically include disease monitoring, crop staging, and weather forecasting with the objective of maximizing marketable yield, minimizing the use of fungicide applications and minimizing the risk of disease resistance. DuPont Acapela Fungicide is compatible with current IPM strategies and provides another alternative to currently registered fungicides. It is expected that growers will be able to integrate the use of DuPont Acapela Fungicide into existing fungicide application plans.

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

DuPont Acapela Fungicide is a fungicide from the Strobilurin - methoxyacrylate chemical class. Picoxystrobin has a mode of action similar to some fungicides currently on the market. This QoI fungicide acts at the quinone outer binding site of the cytochrome bc1 complex. All members of this group affect the Qo site of the cytochrome bc1 complex in mitochondria and inhibit respiration. Picoxystrobin has the same general target site as other strobilurin fungicides, so the development of a spray program employing proper alternation with different modes of action is essential.

DuPont Acapela Fungicide may be used in mixtures with fungicides that have different modes of action or in rotational programs with products from different mode of action groups. It may be used as a component of an integrated disease management program. Product labels and directions for use will include appropriate disease resistance management statements and guidelines for rotation and alternating different mode of action chemicals for disease control.

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, picoxystrobin and its 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:

- Picoxystrobin does not meet Track 1 criteria, and is not considered a Track 1 substance. See Appendix I, Table 19 for comparison with Track 1 criteria.

- Log K_{OW} information is required for the five transformation products Compounds 2, 3, 7, 8 and 26 to confirm that they are not bioaccumulative according to the TSMP Track 1 criterion.

- To assess the volatile transformation product, Compound 26, against the TSMP Track 1 criteria and to assess whether it is likely to undergo long-range transport, information on the octanol-air partition coefficient (log K_{OA}) and on the phototransformation in air of Compound 26 is required.

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*

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:

> Technical grade picoxystrobin does not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*
>
> The end-use product, DuPont Acapela Fungicide, contains the preservative 1,2-benzisothiazoline-3-one which contains low levels of dioxins and furans. These are being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of TSMP.
>
> The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02[9].

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for picoxystrobin is adequate to define the majority of toxic effects that may result from exposure. There was no evidence of increased susceptibility of the young in reproduction or developmental toxicity studies. In short-term and chronic studies on laboratory animals, the primary target was the G.I. tract, resulting in irritation and reduced body weights. There was evidence of neurotoxicity. There was evidence of testicular oncogenicity in rats after longer-term dosing, but only in the presence of overt toxicity. 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 picoxystrobin in plant and livestock commodities. The proposed use of picoxystrobin on dry legumes (Crop Subgroup 6C), cereals (barley, buckwheat, millet, oats, rye, teosinte, triticale and wheat), corn (field, sweet, seed and popcorn) and soybeans does not constitute an unacceptable acute or chronic dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits.

Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.

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.

The PMRA recommends that the following maximum residue limits be specified for:

Commodity	Recommended MRL (ppm)
Barley bran	0.5
Barley	0.3
Wheat germ	0.09
Crop Subgroup 20A (Rapeseed Subgroup)	0.08
Corn oil	0.07
Crop Subgroup 6C (Dried Shelled Pea and Bean, except soybean)	0.06
Wheat bran	0.06
Dry soybeans	0.05
Crop Group 15 (Cereal Grains, except barley and rice)	0.04
Eggs	0.01
Fat, meat and meat by-products of cattle, goats, hogs, horses, poultry, and sheep	0.01
Milk	0.01

Mixers, loaders, and applicators handling DuPont Acapela Fungicide and workers entering treated areas are not expected to be exposed to levels of picoxystrobin that will result in an unacceptable risk when the products are used according to label directions. The personal protective equipment on the product label is adequate to protect workers. Additionally, no risks of concern were identified for bystanders.

7.2 Environmental Risk

The use of DuPont Acapela Fungicide containing the active ingredient picoxystrobin may pose a risk to earthworms, beneficial predatory and parasitic arthropods, non-target terrestrial plants and freshwater invertebrates, fish, amphibians and algae. Risks can be mitigated with spray buffer zones to protect sensitive terrestrial and aquatic habitats from spray drift and through the use of label statements to inform users of potential risks to the environment.

7.3 Value

The data submitted to register DuPont Acapela Fungicide are adequate to demonstrate efficacy for use on the proposed crops and diseases. The lowest effective rate for pests has been established and is supported by efficacy data. Confirmatory data are required to confirm the level of efficacy of picoxystrobin on several crops. Please refer to Appendix I, Table 21 for a summary of supported use claims.

The Canadian Grower Priority Database (CGPD) compiles and prioritizes grower-identified priorities for crop pest protection. Growers have identified the following low, intermediate and high priorities for registration of new fungicides: control of powdery mildew, rust diseases and *Septoria* diseases on cereals; control of northern corn leaf blight and common rust on corn; control of *Sclerotinia* on legumes; control of *Sclerotinia* and *Septoria* diseases on soybean. These priorities correspond to the uses that are proposed for picoxystrobin.

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 Picoxystrobin Technical Fungicide and DuPont Acapela Fungicide, containing the technical grade active ingredient picoxystrobin, to control or suppress a broad spectrum of diseases on cereals, corn, dry legumes and soybeans. 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
a.i.	active ingredient
abs	absolute
AD	administered dose
ADI	acceptable daily intake
AGF	aspirated grain fractions
AR	applied radioactivity
ARfD	acute reference dose
ARTF	Agricultural Re-entry Task Force
atm	atmosphere
ATPD	area treated per day
$AUC_{(0-\infty)}$	area under the curve
BAF	bioaccumulation factor
BBCH	Biologische Bundesanstalt, Bundessortenamt and Chemical Industry
BCF	bioconcentration factor
bw	body weight
bwg	body weight gain
C_{max}	maximum concentrations
C.I.	confidence interval
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CGPD	Canadian Grower Priority Database
cm	centimetres
COC	crop oil concentrates
d	day(s)
DAT	days after treatment
DEEM	Dietary Exposure Evaluation Method
DFR	dislodgeable foliar residue
DFOP	double first order in parallel
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)
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated dietary exposure
EEC	estimated environmental concentration
EPA	Environmental Protection Agency
ER_{25}	effective rate for 25% of the population
F_1	first generation
F_2	second generation
fc	food consumption
FDA	*Food and Drugs Act*
fe	food efficiency
FIR	food ingestion rate

g	gram
G.I.	gastrointestinal
GSD	geometric standard deviation
ha	hectare(s)
HAFT	highest average field trial
HC	historical controls
HC_5	harzardous concentration to 5% of the species
HDPE	high-density polyethylene
HPLC	high performance liquid chromatography
hr/hrs	hour/hours
IgM	immunoglobin M
i.m.p.	initial measured parent
int	interim
IORE	indeterminate order rate equation
IPM	Integrated Pest Management
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_{OA}	octanol-air partition coefficient
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
kPa	kilopascals
L	litre
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
LOD	limit of detection
LOQ	limit of quantitation
LPH	low pressure handwand
LR_{50}	lethal rate 50%
m	metre(s)
MAS	maximum average score for 24, 48 and 72 hours
MBD	more balanced diet
mg	milligram(s)
MI	Michigan
MIS	maximum irritation score
mL	millilitre(s)
M/L/A	mixer/loader/applicator
MMAD	mass median aerodynamic diameter
MOE	margin of exposure
mPa	millipascals
MRL	maximum residue limit
MS	mass spectrometry
MTD	maximum tolerated dose
N	nitrogen

N/A	not applicable
NAFTA	North American Free Trade Agreement
NC	North Carolina
ng	nanograms
nm	nanometres
NOAEL	no observed adverse effect level
NOAEEC	no observed adverse ecological effect concentration
NOEC	no observed effect concentration
NOEL	no observed effect level
NR	not reported
NZW	New Zealand white
OECD	Organisation for Economic Co-Operation and Development
Pa	pascals
PA	Pennsylvania
PBI	plantback interval
PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PND	postnatal day
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
QoI	quinine outside inhibitor
RAC	raw agricultural commodity
REI	restrictive entry interval
rel	relative
RQ	risk quotient
RSD	relative standard deviation
sac	sacrifice
SC	soluble concentrate
SFO	single first-order
sRBC	sheep red blood cell
SSD	species sensitivity distribution
$T_{1/2elim}$	terminal elimination half-life
TC	transfer coefficient
ter	terminal
TGAI	technical grade active ingredient
T_{max}	time to maximum concentrations
TRIG	triglycerides
TRR	total radioactive residue
TRT	treatment
TSMP	Toxic Substances Management Policy
UK	United Kingdom
US	United States
US EPA	United States Environmental Protection Agency

UV	ultraviolet
v/v	volume per volume dilution
w/v	weight per volume dilution
wk/wks	week/weeks
wt/wts	weight/weights
yr/yrs	year/years

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Soil		picoxystrobin IN-QDK50 IN-QDK62 IN-QDK63	HPLC-MS/MS	0.01 ppm	1966841 1893553 1893554 1893555 1893556
Sediment	Extended from soil				
Water		picoxystrobin		0.10 ppb	1893557 1893558 1893559

Analytical Methodology	
Parameters	**Plant Matrices**
Method ID	Du-Pont-29312
Type	LC-MS/MS
Analytes	Picoxystrobin, IN-QDK50, IN-QDY62, and IN-QDY63
LOQ	0.01 ppm/analyte (five distinct crop types)
References	PMRA# 1893767, 1893768 and 1893769
Parameters	**Animal Matrices**
Method ID	Du-Pont-25997, Revision No. 1
Type	LC-MS/MS
Analytes	Picoxystrobin
References	PMRA# 1893763 and 1893765

Table 2 Toxicity Profile of End-use Product DuPont Acapela 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 Toxicity Study Alpk:AP$_f$SD rats PMRA 1893818; MRID 48073720	LD_{50} ♂ > 2000 mg/kg bw LD_{50} ♀ > 2000 mg/kg bw LD_{50} ♂♀ > 2000 mg/kg bw **Limit Dose** **Low Toxicity**
Acute Dermal Toxicity Study Alpk:AP$_f$SD rats PMRA 1893819; MRID 48073722	LD_{50} ♂ > 2000 mg/kg bw LD_{50} ♀ > 2000 mg/kg bw LD_{50} ♂♀ > 2000 mg/kg bw **Limit Dose** **Low Toxicity**
Acute Inhalation Toxicity Study Sprague Dawley derived, albino rats PMRA 1893820; MRID 48073724	Inhalation LC_{50} ♂ > 5.31 mg/L Inhalation LC_{50} ♀ > 5.31 mg/L Inhalation LC_{50} ♂♀ > 5.31 mg/L **Limit Dose** **Low Toxicity**

Study Type/Animal/PMRA #	Study Results
Eye Irritation NZW rabbits PMRA 1893821; MRID 48073726	MIS (2hrs) 4.67/110 MAS (24 – 72 hrs) 0.67/110 Time to zero score 72 hrs **Minimally irritating**
Dermal Irritation MZW Rabbits PMRA 1893822; MRID 48073728	MAS (24 – 72 hrs) 1.33/8 **Slightly irritating**
Dermal Sensitization Study Albino Dunkin Hartley Guinea Pigs PMRA 1893823; MRID 48073730	2/20 exhibited signs of sensitization at the undiluted treatment sites 0/20 exhibited signs of sensitization at the 75% w/v test site **Not a dermal sensitizer**

Table 3 Toxicity Profile of Technical Picoxystrobin

(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 Toxicity (Up and Down) Crl:CD(SD) rats PMRA 1893595; MRID 48073718	LD_{50} > 5000 mg/kg bw **Limit Dose** **Low Toxicity**
Acute Dermal Toxicity Crl:CD(SD) rats PMRA 1893596; MRID 48073721	LD_{50} > 5000 mg/kg bw **Limit Dose** **Low Toxicity**
Acute Inhalation Toxicity Wistar / CRL:WI rats PMRA 2027703; MRID 48405401	LC_{50} = 0.11 mg/L (C.I. = 0.011 – 0.20 mg/L) **Moderately acutely toxic** 0.019 mg/L: red foci on lobes of lungs ♂; diaphragmatic nodule ♀ 0.16 mg/L:3/5 ♂ and 4/5 ♀ exhibited dullness and died, enlarged, edematous lungs and frothy fluid in trachea, congested lung lobes; clotted blood in abdominal cavity ♂ 0.42 mg/L: 5/5 ♂ and 4/5 ♀ exhibited dullness and died, enlarged, edematous lungs
Eye Irritation Study NZW Rabbit PMRA 1893599; MRID 48073725	Supplementary MIS (24hrs) 27/110; MAS (24-72) 17.7/110 Score at 7 days = 0/110
Eye irritation Study	MAS (1-48 hrs) 6.7/110; MIS (1 hr) 11.7/110

Study Type/Animal/PMRA #	Study Results
NZW Rabbits PMRA 2092925; MRID 2092925	Score at 72 hours = 2.67/110 Score at 7 days = 2/110 **Mildly irritating to the eye**
Dermal Irritation Study NZW Rabbit PMRA 1893597; MRID 48073727	MAS 0/8 **Non-irritating**
Dermal Sensitization Study Hartley Albino Guinea Pig PMRA 1893598; MRID 48073729	There were no reactions following an undiluted challenge **Not a skin sensitizer**
Metabolism/Toxicokinetics (single and repeated dose, oral, gavage) Wistar rats PMRA 1893661; MRID 48073755 PMRA 1893664; MRID 48073756 PMRA 1893668; MRID 48073757 PMRA 1893669; MRID 48073758 PMRA 1893670; MRID 48073759 PMRA 1893671; MRID 48073754	Studies were conducted with [^{14}C-pyridinyl]- or [^{14}C-phenyl]- picoxystrobin [^{14}C-phenyl]picoxystrobin and [^{14}C-pyridinyl]picoxystrobin were examined for biotransformation, excretion and tissue distribution in five studies. Picoxystrobin is well absorbed (77-82%) and completely excreted (94-100%). The majority is excreted in the feces (74-78% in ♂ and 61-65% in ♀) with bile as the primary route and 18-21% and 26-34% excreted in the urine in ♂ and ♀, respectively. At 120 hours post-dose the highest concentrations of residual radioactivity (TRR) were in the liver, followed by the kidneys and G.I tract. All other organs have TRR levels lower than whole blood. At 24 hours post-dose, whole body radiographs indicated that the highest concentrations of TRR were in the G.I tract, liver and kidneys in descending order. Picoxystrobin was well distributed with TRR levels found in the bone as well as G.I organs. Picoxystrobin was extensively metabolized and well characterized. Thirty-four of 42 identified metabolites were structurally identified. The parent compound was only found in the feces and the major metabolite in the bile cannulation study was not found in the urine or feces. The major route of metabolism was via ester hydrolysis and glucuronide conjugation. Plasma kinetic investigations of picoxystrobin found a general similarity between sexes, radiolabels and dose groups, though there was a high degree of variability between individual rats. C_{max} values in plasma were between 2.35-4.36 µg/g at low doses and 8.89-10.84 µg/g at high doses. The T_{max} generally occurred at 0.5-1.0 hours post-dose at low doses and at 24 hours for high doses when the data from the two labels was pooled; however, there was a high degree of variability due to two peaks of radioactivity in the concentration vs time curves at 1 and 8-24 hours post-dosing. These peaks are probably a result of enterohepatic circulation of metabolites supported by earlier bile cannulation studies. Single oral low and high-dose studies were performed with the ^{14}C-phenyl and ^{14}C-pyridinyl rings at 10 and 100 mg/kg bw. Terminal elimination half-lives ($T_{½elim}$) was 33.4-47.2 hrs at low doses and 30.5-45.8 hrs at high doses. The major sex difference was area under the curve ($AUC_{(0-\infty)}$) values of 101.8-110.2 hr*µg/g in ♂ at low dose and 85.9-86.7 hr*µg/g in ♀. At high doses, the $AUC_{(0-\infty)}$ was 579.3-605.0 hr*µg/g and 453.4-709.6 hr*µg/g in ♂ and ♀, respectively. A 5.2-8.3 fold difference in AUC between the low and high doses indicates that metabolism may be reaching saturation at high doses.
90d Oral Toxicity Study C57BL/10JfAP/Alpk mice PMRA 1893680; MRID 48073732	Effect levels were not established since this was a supplemental study Non-guideline; no clinical chemistry, haematology, organ weights or histopathology ≥ 137.3/176.1 mg/kg bw/day: ↓ bw/bwg and fe 421.6/534.8 mg/kg bw/day: dark areas, dark spots on spleen, ↑ pigmentation in spleen
90d Oral Toxicity Study Alpk:AP$_f$SD rats	**NOAEL - 41.7/48.1 mg/kg bw/day** 104.9/120.1 mg/kg bw/day: ↓ bw/bwg and fc

Study Type/Animal/PMRA #	Study Results
PMRA 1893674; MRID 48073731	
90d dietary toxicity study Beagle dogs PRMA 1893676; MRID 48073734	**NOAEL - 8.9/8.5 mg/kg bw/day** 16.5/16.9 mg/kg bw/day: ↓ fc and ↑ fluid feces in ♂(18 observations, wk 1 – 13)♀(6 observations, wk 1-3 and 12-13); ↓ bw/bwg in ♂; ↑ salivation at feeding in ♀ (wk 2 – 13)
28d dermal toxicity study Crl:CD(SD) rats PMRA 1893682; MRID 48073735	**NOAEL - 1000 mg/kg bw/day**
28d dermal toxicity study Alpk:AP$_f$SD rats PMRA 1893678; MRID 48073736	**NOAEL 1000 mg/kg bw/day**
1yr dietary toxicity study Beagle dogs PMRA 1893621; MRID 48073741	**NOAEL 4.8/4.6 mg/kg bw/day** ≥ 16.1/15.7 mg/kg bw/day: ↓ bw/bwg and fc; ↑ salivation and red sclera in ♂
18 month Dietary Toxicity Study C57BL/10J$_f$ AP Alpk mice PMRA 1893602; MRID 48073744	Supplementary; did not reach MTD 108.8/144.7 mg/kg bw/day: ↑ incidence of inflammation and erosion in non-glandular stomach in ♀ (same severity as controls)
18 month Dietary Toxicity Study Crlj:CD1 (ICR) mice PMRA 2046231; MRID 48457401	**NOAEL 70.8/98.6 mg/kg bw/day** ≥ 293.3/411.5 mg/kg bw/day: ↑ hyperplasia of duodenal mucosa, ↑ dilatation of mucosal glands and ↑ incidence of stomach glandular mucosal hyperplasia ♂ Did not reach MTD, but approached limit dose in females. No evidence of tumours
2yr Dietary Toxicity Study Alpk:AP$_f$ SD rats PMRA 1893610; MRID 438073746	Supplementary; did not reach MTD No effects at 45.6/57.8 mg/kg bw/day (highest dose tested)
2yr Dietary Toxicity Study CD® [Crl:CD®(SD)] rats PMRA 2046238; MRID 48457202	**NOAEL 52.3/65.0 mg/kg bw/day** ≥ 52.3/65.0 mg/kg bw/day: ↑ incidence of soft feces (non-adverse) ♂ ≥ 186.3/229.6 mg/kg bw/day: ↓ bw/bwg; ↑ incidence of soft feces; ↑ testes wts (int sac), ↑ incidence interstitial cell hyperplasia and adenomas of testes (ter sac) ♂; ↑ urea N, ↓ TRIG ♀ Adenoma, testicular interstitial cell: ♂: 1/70 (1.4), 1/70 (1.4), 0/70, 2/70 (3.0), 7/70 (10) HC: 0 – 8.3
Reproductive Toxicity Study Sprague-Dawley (Crl:CD[SD]) rats PMRA 1893640; MRID 48073739	Parental Toxicity **NOAEL 55.5/70.3mg/kg bw/day** 137.5/173.4 mg/kg bw/day: ↓ bw/bwg, fc and food efficiency Offspring Toxicity **NOAEL 16.9/21.7 mg/kg bw/day** ≥ 55.5/70.3 mg/kg bw/day: ↓ abs spleen wts F_1&F_2

Study Type/Animal/PMRA #	Study Results
	Reproductive Toxicity **NOAEL 137.5/173.4 mg/kg bw/day**
Reproductive Toxicity Study Alpk:AP$_f$SD rats PMRA 1893638; MRID 48073740	Parental Toxicity **NOAEL 5.4/5.8 mg/kg bw/day** ≥ 21.5/23.4 mg/kg bw/day: ↓ bw/bwg, fc F_1 ♂ Offspring Toxicity **NOAEL 21.5/23.4 mg/kg bw/day** 80.0/87.2 mg/kg bw/day: ↓bw F_1 @ PND 29, F_2 @ PND 22 & 29 Reproductive Toxicity **NOAEL 80.0/87.2 mg/kg bw/day**
Developmental Toxicity Study Alpk:AP$_f$SD (Wistar-derived) rats PMRA 1893636; MRID 48073738	Maternal Toxicity **NOAEL 30 mg/kg bw/day** 100 mg/kg bw/day: ↓bwg, ↑ diarrhea and post-dosing salivation Offspring Toxicity: **NOAEL 30 mg/kg bw/day** 100 mg/kg bw/day: extremely misaligned 5th sternebra
Developmental Toxicity Study NZW rabbits PMRA 1893647; MRID 48073737	Maternal Toxicity **NOAEL 8 mg/kg bw/day** ≥25 mg/kg bw/day: ↑ diarrhea, ↑ incidences few feces on tray, ↓ fc, ↓ gravid uterine wts Developmental Toxicity: **NOAEL 25 mg/kg bw/day** 100 mg/kg bw/day: incomplete ossification of the odontoid and presence of 27 pre-pelvic vertebrae
Bacterial Reverse Mutation Assay PMRA 1893655; MRID 48073748	**Negative** Precipitation at ≥ 2500 µg/plate (plate incorporation) and 5000 µg/plate (pre-incubation)
In vitro Mammalian Cell Assay PMRA 1893656; MRID 48073747	**Negative** Precipitation at ≥ 64 µg/mL
In vitro Mammaliam cell clastogenicity PMRA 1893565; MRID 48073749	**Negative** Cytotoxic at 5µg/mL –S9 and 50 µg/mL +S9
In vivo Cytogenetics (MN Assay) PMRA 1893660; MRID 48073750	**Negative**
In vivo Rat Liver Unscheduled DNA Synthesis Assay PMRA 1893659; MRID 48073751	**Negative**
Acute Neurotoxicity Study Crl:CD(SD) rats PMRA 1893600; MRID 48073753	**NOAEL not established** ≥ 200 mg/kg bw/d: low arousal and reduced motor activity ♂, reduction in rearing ♀ ≥ 1000 mg/kg bw/d: ↓ fc, ↑ stained skin/fur, drooping eyelids; diarrhea, brown-stained cageboard, curled-up posture, low arousal; low body temperature, high carriage ♀ 2000 mg/kg bw/d: soiled/wet skin/fur; low body temperature ♂; 3 ♀ found dead/moribund, red nasal discharge, uncoordinated gait, abnormal posture ♀
Subchronic Neurotoxicity Study Crl:CD(SD) rats PMRA 1893681; MRID 48073752	**NOAEL 8 mg/kg bw/d in females; 36 mg/kg bw/d in males** ≥36/46 mg/kg bw/day: ↓ bw/bwg ♀ 207/246 mg/kg bw/day: ↓fc; ↓ bw/bwg, ↓ forelimb grip strength ♂; ↓ landing foot splay ♀
Immunotoxicity Study	Immunotoxicity (IgM response to Sheep Red Blood Cell (sRBC)) **NOAEL 231/225 mg/kg bw/day**

Study Type/Animal/PMRA #	Study Results
CRL:CD(SD) rats PMRA 1893672; MRID 48073762	 Systemic Toxicity **NOAEL 68/75 mg/kg bw/day** 231/225 mg/kg bw/day: ↓ bw/bwg; ↓fc ♀
Immunotoxicity Study CRl:CD1(ICR) mice PMRA 1893673; MRID 48073763	Immunotoxicity (IgM response to sRBC) **NOAEL 727/931 mg/kg bw/day** Systemic Toxicity: **NOAEL 727/931 mg/kg bw/day**
Metabolite Studies	
Acute Inhalation Toxicity Study Wistar (Alpk:AP$_f$SD) rats PMRA 1966847; MRID 48258033	≥ 5.29 mg/L: ↑ breathing depth, abnormal respiratory noise, ↓ activity, ↓ righting reflex, ↑ salivation, ↓ stability, ↓ response to sound, ↑ shaking, ↓ foot withdrawl reflex; asymptomatic by Day 5 ≥ 10.48 mg/L: ↓ body weight in 2/5 ♀; coldness to touch, ↓ splay and visual placing reflexes, ↑ palpebral and pinna reflexes, ↑ staining around snout; asymptomatic by Day 5 26.24 mg/L: 2/5 ♀ died immediately post-exposure; 2/5 ♂ lost weight in first week, 1/5 ♀ lost weight in first week and 1/5 ♀ lost weight throughout study; ↓ breathing rate, ↑ lacryimation, ↑ prostrate posture; asymptomatic by Day 7 in surviving animals; 1/2 decedent ♀ with red lungs MMAD and GSD were not provided

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

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary general population	Acute rat oral neurotoxicity study	LOAEL = 200 mg/kg bw Low arousal and reduced motor activity in males and reduction in rearing in females	300
	ARfD = 0.67 mg/kg bw		
Repeated dietary	1-year dog dietary study	NOAEL = 4.6 mg/kg bw/day Decreased body weight, body weight gain and food consumption in males and females and increased salivation and red sclera in males	100
	ADI = 0.046 mg/kg bw/day		
Short and Intermediate-term dermal	The two 28-day rat dermal studies	NOAEL = 1000 mg/kg bw/day No treatment-related effects at highest dose tested	100
Short and Intermediate-term inhalation[2]	90-day dog dietary toxicity study	NOAEL 8.5 mg/kg bw/day Increased fluid feces in males and females, decreased body weight and body weight gain in males, and increased salivation at feeding in females	100
Cancer	Combined chronic/oncogenicity dietary study in rats	A threshold-based approach was used for testicular interstitial adenomas in male rats	N/A

[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments; MOE refers to a target MOE for occupational assessments.

[2] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation.

Table 5 Integrated Food Residue Chemistry Summary

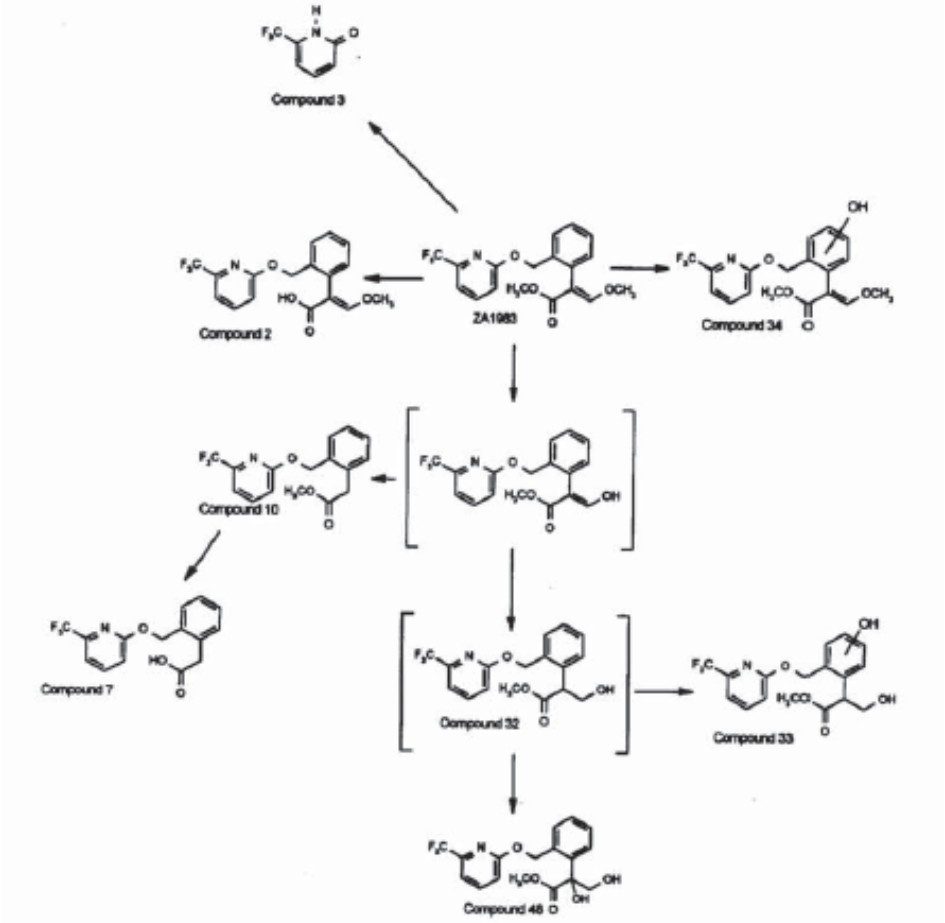
NATURE OF THE RESIDUE IN ANIMALS - Hen	PMRA# 1893592
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenyacrylate-^{14}C] Picoxystrobin**

Laying hens (two groups with 3 birds per treatment group) were dosed orally twice daily with either [pyridinyl-^{14}C] or [phenylacrylate-^{14}C] picoxystrobin at a rate of 10 ppm in the feed for 10 consecutive days. Samples of excreta were collected daily. Samples of eggs were collected twice daily. The treated hens were sacrificed approximately 16 hours after the final dosage and samples of liver, muscle and fat were collected.

Matrices	[pyridinyl-^{14}C]		[phenylacrylate-^{14}C]	
	TRRs (ppm)	% AD	TRRs (ppm)	% AD
Excreta	NR	64.73	NR	93.77
Cage wash	NR	2.68	NR	1.88
Egg yolk (Day 10)	0.209	0.10	0.192	0.08
Egg white (Day 10)	0.015	0.02	0.005	0.01
Muscle	0.019	0.04	0.022	0.05
Fat	0.054	0.02	0.046	0.01
Liver	0.173	0.07	0.31	0.14
Total % AD	67.66		95.93	

Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**
Egg yolk	None	None	Picoxystrobin, Compounds 3, 7 and 10	Picoxystrobin and Compound 7

Proposed metabolic scheme in hens:



Picoxystrobin was metabolized to Compound 2 or Compound 34 directly. Other intermediates were also proposed and these intermediates were transformed to Compound 10, or Compound 33 and Compound 48.

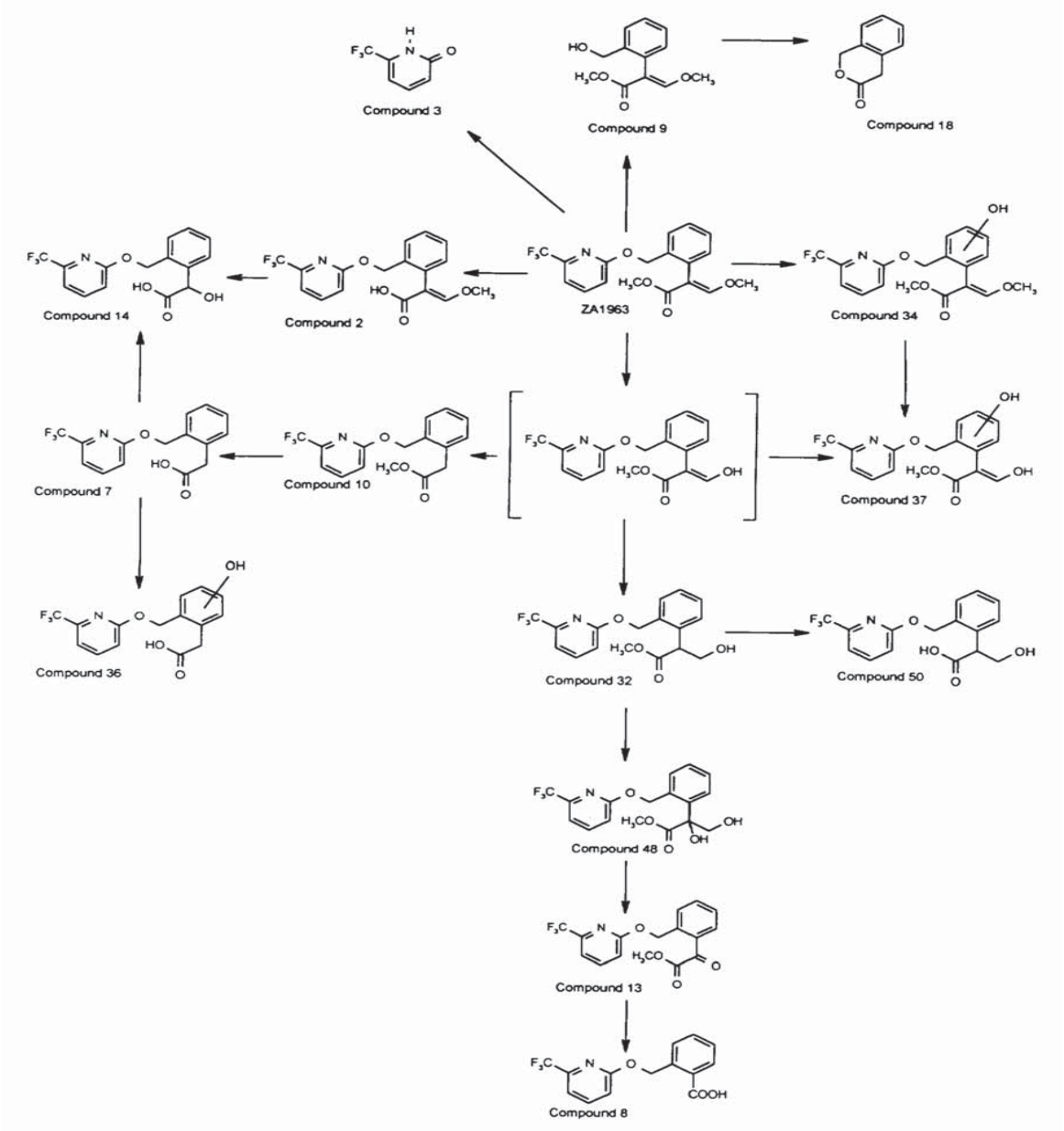
NATURE OF THE RESIDUE IN ANIMALS - Goat	**PMRA# 1893593**
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenyacrylate-^{14}C] Picoxystrobin**

Lactating goats (one animal for each treatment) were dosed orally twice daily with either [pyridinyl-^{14}C] or [phenylacrylate-^{14}C] pycoxystrobin at a rate of 10 ppm in the feed for 7 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 about 16 hours after the last dose.

Matrices	[pyridinyl-^{14}C]		[phenylacrylate-^{14}C]	
	TRRs (ppm)	% AD	TRRs (ppm)	% AD
Bile	0.845	0.03	5.100	0.11
Bladder Urine	NR	No samples	6.195	0.24
Omental fat	0.034	NR	0.025	NR
Perirenal fat	0.028	NR	0.026	NR
Subcutaneous fat	0.033	NR	0.021	NR
Kidney	0.057	0.01	0.149	0.02
Liver	0.115	0.11	0.340	0.20
Muscle (Hind)	0.006	NR	0.010	NR
Muscle (Fore)	0.007	NR	0.009	NR
G.I. tract	0.255	2.03	0.484	2.76
Whole Blood	0.025	NR	0.058	NR
Plasma	0.033	NR	0.073	NR
Urine (pooled)	NR	46.32	NR	49.41
Feces (pooled)	NR	35.61	NR	27.28
Cage wash (pooled)	NR	0.67	NR	1.59
Milk (pooled)	NR	0.20	NR	0.06
Total % of AD	85.03		81.67	

Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**
Liver	None	None	Picoxystrobin, Compounds 2, 3, 7, 8, 10, 13, 32, 34, 36, 48, and 50	Picoxystrobin, Compounds 2, 7, 9, 10, 13, 14, 18, 32, 34, 36, 48, and 50
Kidney	Compound 7 (0.008 ppm)	Compound 7 (0.020 ppm)	Picoxystrobin, Compounds 2, 8, 10, 13, 32, 34, 48, and 50	Picoxystrobin, Compounds 2, 8, 9, 10, 13, 32, 34, 48, and 50
Omental fat	Picoxystrobin	Picoxystrobin	None	None
Perirenal fat	Picoxystrobin	Picoxystrobin	None	None
Subcutaneous fat	Picoxystrobin	Picoxystrobin	None	None

Proposed metabolic scheme in goats:



Picoxystrobin metabolism in goats proceeds through hydrolysis or cleavage to form Compound 2 or Compound 9, which may then undergo further metabolism to yield Compound 14 and Compound 18. Other possible metabolic pathways involve formation of Compound 34 or Compound 10, which further transform to various other metabolites.

NATURE OF THE RESIDUE IN PLANTS - Wheat	**PMRA# 1893587 and 1893588**
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenylacrylate-^{14}C] Picoxystrobin**
Test site	Outdoors
Treatment	Foliar spray
Rate	Two applications for each label. Pyridinyl label: first application at 437 g a.i./ha, second application at 405 g a.i./ha. Phenylacrylate label: first application at 409 g a.i./ha, second application at 408 g a.i./ha.
Timing	First application: Zadok growth stage of 32. Second application: Zadok growth stage of 65-69.

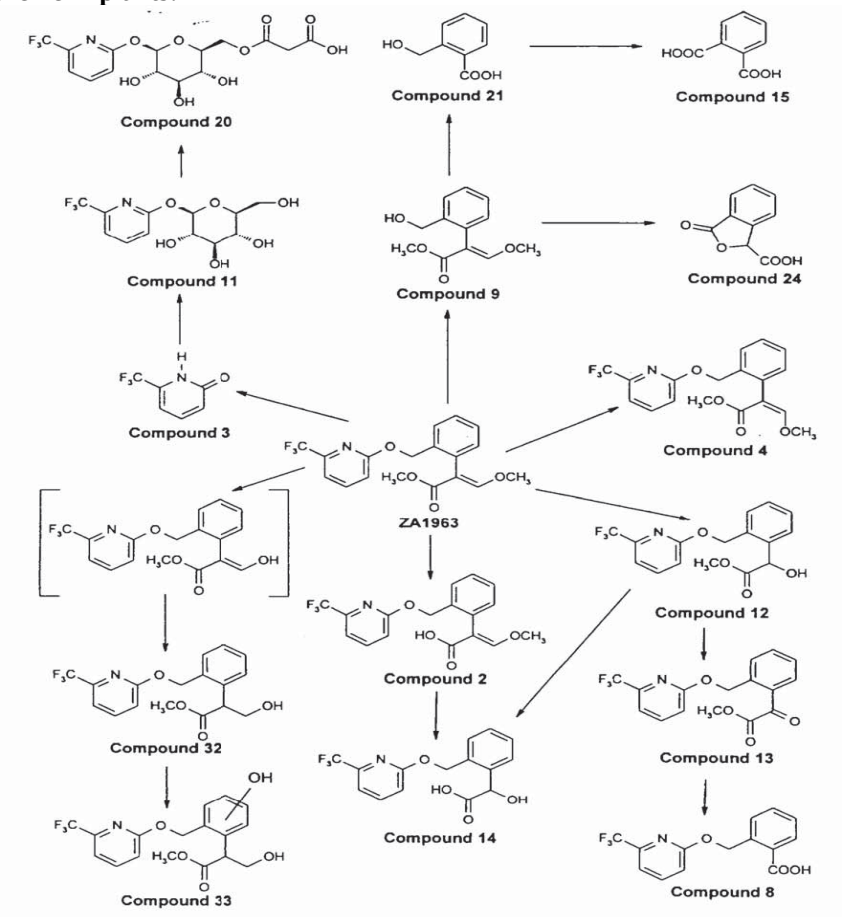
Preharvest interval	Immature forage: 14 days after the last application. Mature straw and grain: 48 days after the last application.
End-use product	Formulated as a suspension concentrate

TRRs in Wheat Raw Agriculture Commodities

Matrix	[pyridinyl-^{14}C] (ppm)	[phenylacrylate-^{14}C] (ppm)
Wheat Forage	3.93	5.89
Wheat Straw	9.90	11.0
Wheat grain	0.081	0.307

Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**
Wheat Forage	Picoxystrobin	Picoxystrobin	Compounds 4, 8, 11, 12, 13, 14, and 20	Compounds 4, 8, 12, 13, 14, 15, 21, and 24
Wheat Straw	Picoxystrobin	Picoxystrobin	Compounds 2, 3, 4, 8, 11, 12, 13 ,14, 32 and 33	Compounds 2, 4, 8, 9, 12, 13 ,14, 15, 21, 24, PAG 3, 32 and 33
Wheat grain	None	Compound 24 (0.046 ppm)	Picoxystrobin	Picoxystrobin, Compounds 15, and PAG 3

Proposed metabolic scheme in plants:



The primary metabolic pathway in wheat appeared to be the hydrolysis of picoxystrobin to form Compound 9, and further transformation to Compound 24 and Compound 15. Hydrolysis of picoxystrobin may also give Compound 2, and further metabolized to Compound 14.

NATURE OF THE RESIDUE IN PLANTS - Canola	**PMRA# 1893591**
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenyl-U-^{14}C] Picoxystrobin**
Test site	Greenhouse
Treatment	Foliar spray

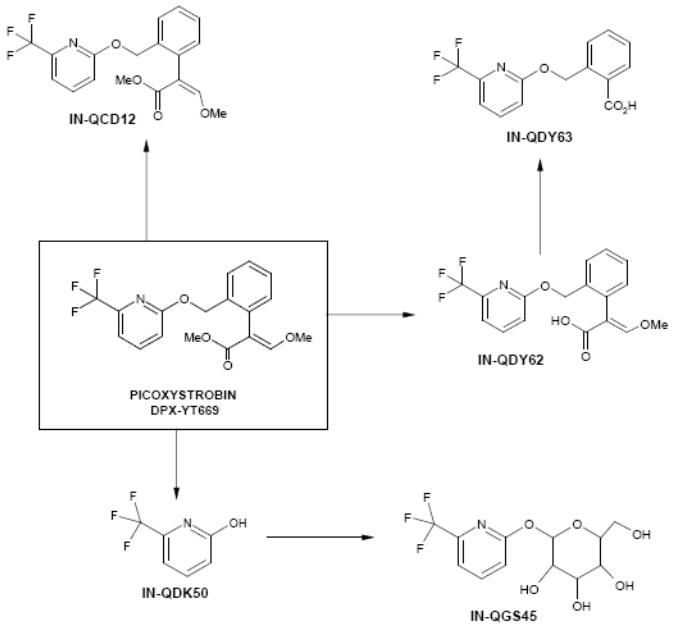
Rate	Two applications for each label. Pyridinyl label: first application at 414 g a.i./ha, second application at 413 g a.i./ha. Phenyl (U) label: first application at 471 g a.i./ha, second application at 471 g a.i./ha.
Timing	First application: BBCH-80 growth stage. Second application: BBCH-85 growth stage, 7 days after the first application.
Preharvest interval	Forage: 7 days after first application, 14 days after the last application, and 21 days after the last application. Seed: 21 days after the last application.
End-use product	Formulated as a suspension concentrate

TRRs in Canola Raw Agriculture Commodities

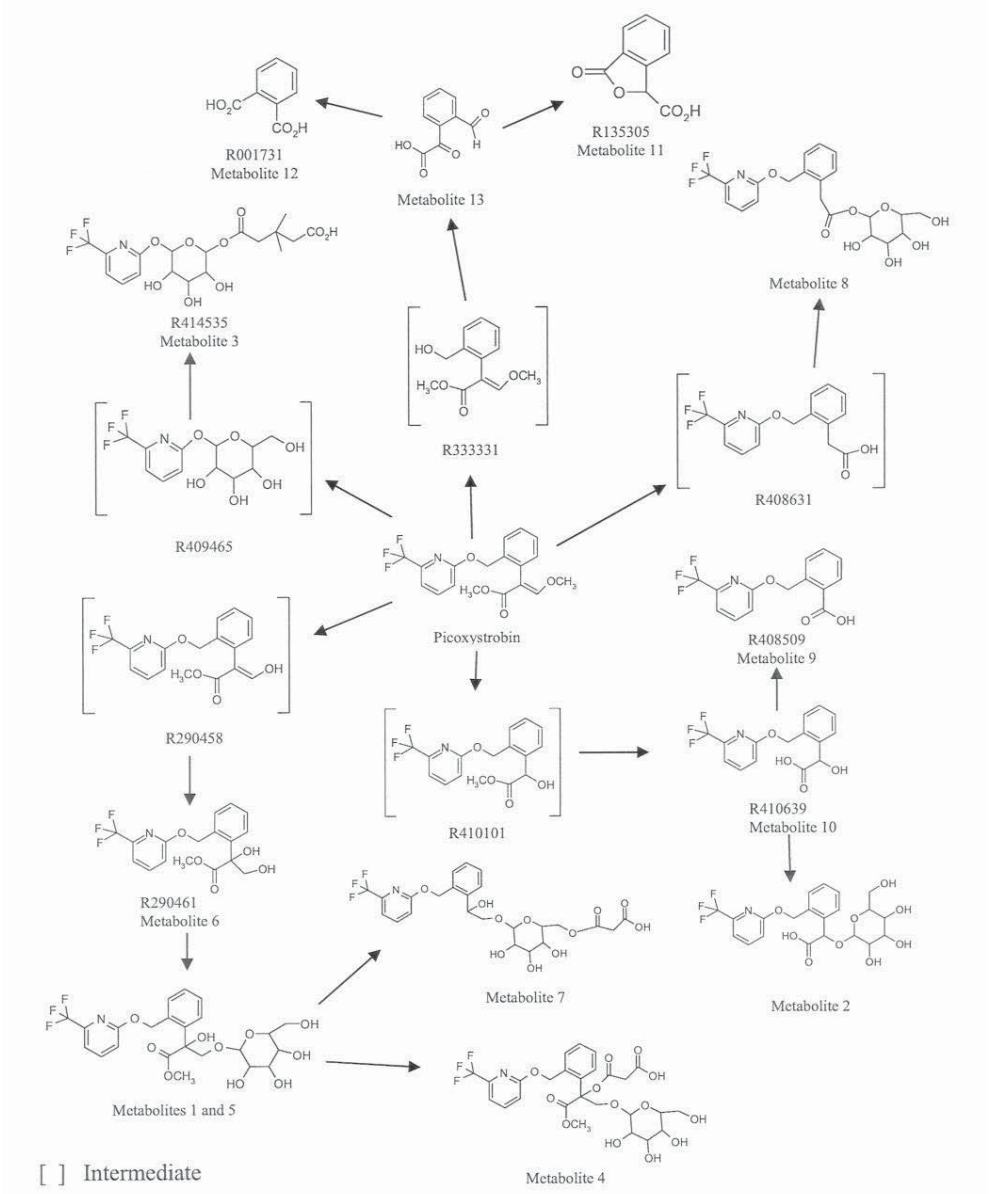
Matrix	[pyridinyl-^{14}C] (ppm)		[phenyl-U-^{14}C] (ppm)	
Foliage/Immature, first harvest	5.93		7.05	
Foliage/Immature, first harvest	12.47		11.52	
Foliage with Pods/Mature	11.80		12.99	
Seed	1.66		2.50	
Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[pyridinyl-^{14}C]**	**[phenyl-U-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenyl-U-^{14}C]**
Immature foliage (7 days after the 1st application)	Picoxystrobin	Picoxystrobin	Compounds 3, 4, and 8	Compound 8
Immature foliage (14 days after the 2nd application)	Picoxystrobin	Picoxystrobin	Compounds 2, 3, 4, and 8	Compounds 2, 4, and 8
Immature foliage (21 days after the 2nd application)	Picoxystrobin	Picoxystrobin	Compounds 2, 3, 4, 8 and 11	Compounds 2, 4, and 8
Seed (21 days after the 2nd application)	Picoxystrobin	Picoxystrobin	None	Compound 4

Proposed metabolic scheme in plants:

Alternative names used:
Picoxystrobin: ZA1963, ZA1963/1, Compound 1, DPY-YT669.
IN-QDY62: Compound 2, R403092
IN-QDY63: Compound 8, R408509
IN-QDK50: Compound 3, R403814
IN-QCD12: Compound 4 (an isomer of picoxystrobin).
IN-QGS45: Compound 11

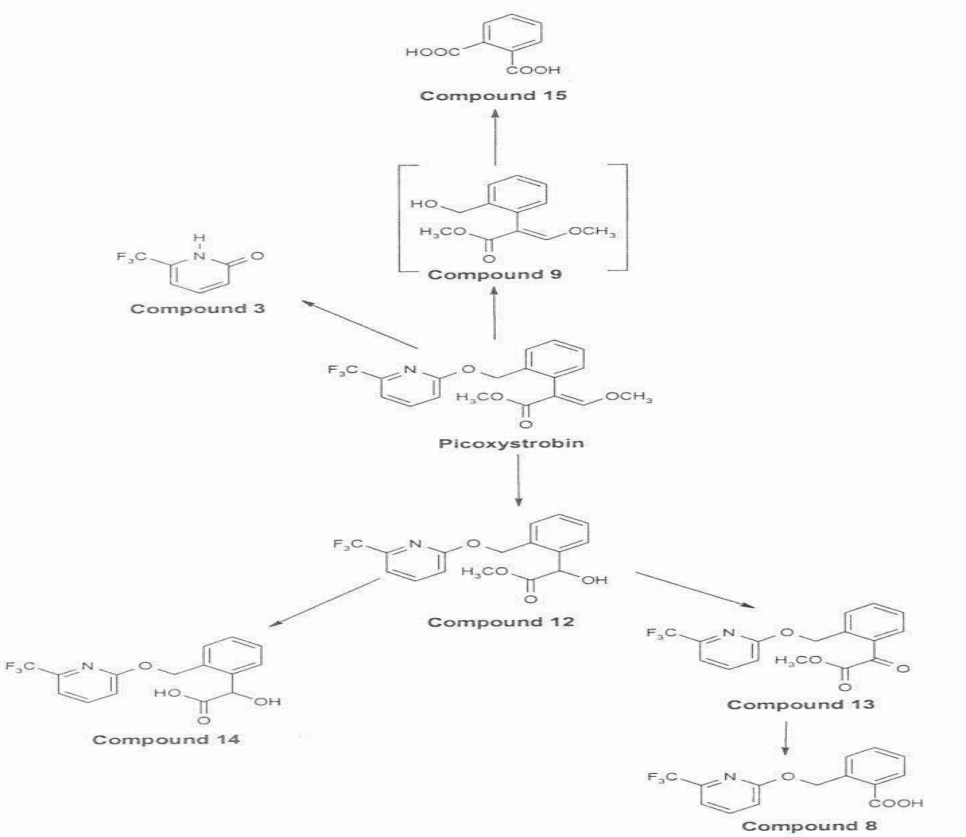


The primary metabolic pathway in canola appeared to be the hydrolysis of picoxystrobin to form Compound 2, and further transformation to Compound 8. Hydrolysis of picoxystrobin may also give Compound 3, and further metabolized to Compound 11.				
NATURE OF THE RESIDUE IN PLANTS - Soybean			**PMRA# 1893589**	
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenyl-U-^{14}C] Picoxystrobin**			
Test site	Outdoors			
Treatment	Foliar spray			
Rate	Two applications at total rates of 200 and 1000 g a.i./ha, respectively, for each label. The rate of 200 g a.i./ha: 100 g a.i./ha for each application The rate of 1000 g a.i./ha: first application at 250 g a.i./ha, second application at 750 g a.i./ha.			
Timing	First application: R3 growth stage. Second application: 14 days after the first application.			
Preharvest interval	Forage: 14 days after the last application. Soybean: 63 days after the last application.			
End-use product	Formulated as a suspension concentrate			
TRRs in Soybean Raw Agriculture Commodities				
Matrix	[pyridinyl-^{14}C] (ppm)		[phenyl-U-^{14}C] (ppm)	
Soybean Forage	1.803		1.896	
Soybean seed	0.080		0.127	
Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[pyridinyl-^{14}C]**	**[phenyl-U-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenyl-U-^{14}C]**
Soybean Forage	Picoxystrobin, M1, M2, M4	M1, M7	M3 and M5	Picoxystrobin, M2, M5, M8, Compound 8, Compound 14, Compound 24, Compound 15
Soybean seed	None	Compound 15 (21.3% TRRs, 0.030 ppm) and M13 (25.5% TRRs, 0.036 ppm)	Picoxystrobin, M1, M2, M3, M4, M5, Compound 48	Picoxystrobin, M1, M2, M7, M8, Compound 8, Compound 14, and Compound 24,
Proposed metabolic scheme in plants: Alternative names used: M6: Compound 48 M9: Compound 8 M10: Compound 14 M11: Compound 24 M12: Compound 15				



NATURE OF THE RESIDUE IN PLANTS - Apples			**PMRA# 1893590**	
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenylacrylate-^{14}C] Picoxystrobin**			
Test site	Outdoors			
Treatment	Foliar spray			
Rate	Three applications at total rates of 180, 180 and 120 g a.i./ha, respectively.			
Timing	First application: BBCH-69 growth stage. Second application: 21 days after the first application. Third application: 85 days after the first application.			
Preharvest interval	Apple: 14 days after the last application.			
End-use product	Formulated as a suspension concentrate			
TRRs in Wheat Raw Agriculture Commodities				
Matrix	[pyridinyl-^{14}C] (ppm)		[phenylacrylate-^{14}C] (ppm)	
Apple	0.064		0.20	
Metabolite Identified	**Major metabolites (>10% TRRs)**		**Minor metabolites (<10% TRRs)**	
Radiolabel Position	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**
Apple	Picoxystrobin	Picoxystrobin	Compounds 3, 12 and 13	Compounds 8, 12, 13, 14 and 15

Proposed metabolic scheme in plants:



The primary metabolic pathway in apples appeared to be the hydrolysis of picoxystrobin to form Compound 9, and further transformation to Compound 15. Hydrolysis of picoxystrobin may also give Compound 12, and further metabolized to Compound 8.

CONFINED ACCUMULATION IN ROTATIONAL CROPS – Spring wheat, winter wheat, carrots and lettuce	**PMRA # 1893815, 1893816, 1893817**
Radiolabel Position	**[Pyridinyl-^{14}C] and [Phenylacrylate-^{14}C] Picoxystrobin**
Test site	Greenhouse and outdoor field plots in UK
Formulation used for trial	10% suspension concentrate
Application rate and timing	820-888 g a.i./ha made to two pots per radiolabel (PBIs of 30 and 197 days) 817-842 g a.i./ha made to the primary crop (winter wheat) per radiolabel (PBI ~305 days) 704-793 g a.i./ha made to the primary crop (spring wheat) per radiolabel (PBI 107 days)

TRRs in Raw Agriculture Commodities

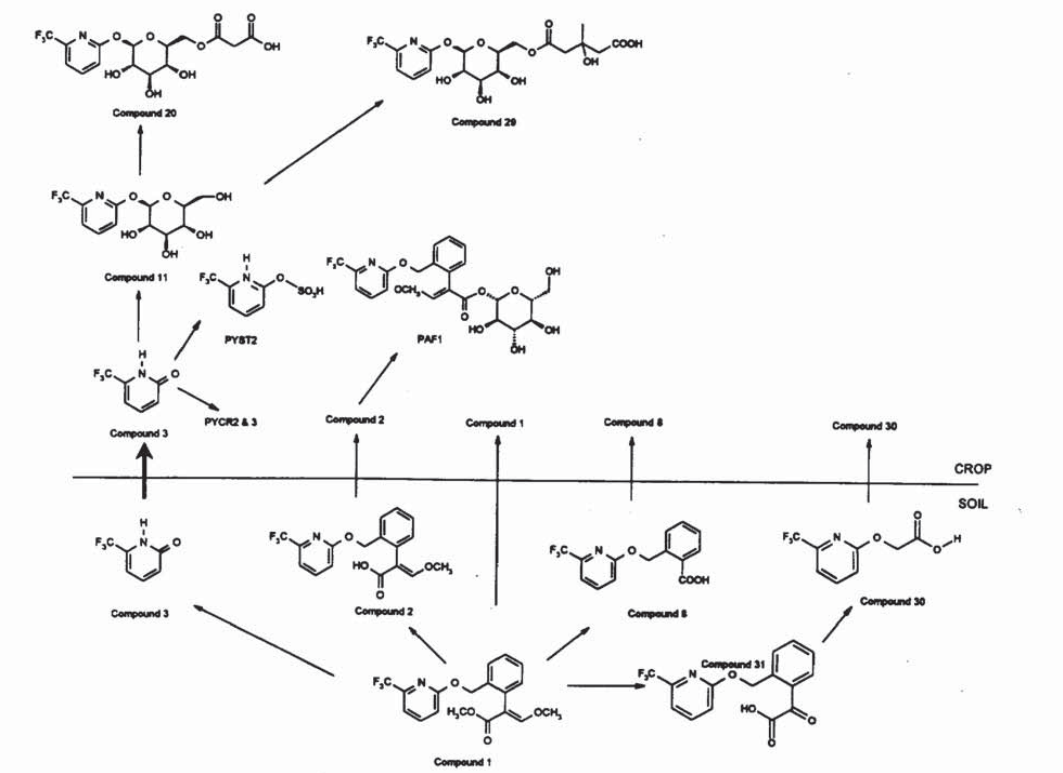
Matrix	PBI (days)	[pyridinyl-^{14}C] (ppm)	[phenylacrylate-^{14}C] (ppm)
Wheat forage (Spring)	30	1.05	0.237
Wheat forage (Winter)	107	0.018	0.010
Wheat forage (Spring)	197	1.04	0.367
Wheat forage (Spring)	305	0.056	0.021
Wheat straw (Spring)	30	12.8	1.93
Wheat straw (Winter)	107	0.082	0.051
Wheat straw (Spring)	197	5.61	1.99
Wheat straw (Spring)	305	0.151	0.025
Wheat grain (Spring)	30	0.073	0.164
Wheat grain (Winter)	107	0.003	0.005
Wheat grain (Spring)	197	0.034	0.084
Wheat grain (Spring)	305	0.003	0.009
Lettuce	30	0.326	0.030
	197	0.222	0.060
	308	0.004	0.001
Carrot foliage	30	1.38	0.078

	197	0.784	0.051
	308	0.048	0.002
Carrot root	30	0.370	0.039
	197	0.212	0.032
	308	0.008	0.001

Metabolites Identified		**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Matrix	**PBI (days)**	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**	**[pyridinyl-^{14}C]**	**[phenylacrylate-^{14}C]**
Wheat forage (immature)	30	Compound 20	Picoxystrobin and PAF1	Picoxystrobin, Compounds 3 and 11	None
	107	Compound 11 and 20	n/a	None	n/a
	197	Compound 20	Compound 30	Picoxystrobin, Compounds 2, 3, 11 and 30	Picoxystrobin
	304	Compound 20	None	Compound 3 and 11	Picoxystrobin
Wheat straw (mature)	30	Compound 3, 20 and PYST2	None	Picoxystrobin, Compounds 2, 11 and 30	Picoxystrobin, Compounds 2, 7 and 30
	107	PYST2	None	Compounds 3, 11 and 20	Compound 8
	197	Compound 20	None	Picoxystrobin, Compounds 2, 3, 11 and 30, PYST2	Picoxystrobin, Compounds 2, 7 and 30
	304	Compound 11	n/a	Compounds 3 and 20	n/a
Wheat grain (mature)	30	Glucose (16.7% TRRs, 0.011 ppm)	None	Compound 3, other natural products	Compound 24, glucose and other natural products
	197	Compound 30 (13.3% TRRs, 0.005 ppm), glucose (12.2% TRRs, 0.002 ppm)	Compound 30 (17.8% TRRs, 0.016 ppm)	Other natural products	Compound 24, glucose and other natural products
Lettuce	30	Compounds 11 and 20	PAF1	Picoxystrobin and Compound 3	Picoxystrobin and Compound 2
	197	Compound 20 (46.3% TRRs, 0.086 ppm)	Compound 30 (31.1% TRRs, 0.014 ppm) and PAF1 (26.6% TRRs, 0.012 ppm)	Picoxystrobin and Compounds 11 and 30	Picoxystrobin
Carrot foliage	30	Compounds 20 and 29	Picoxystrobin and PAF1	Picoxystrobin, Compounds 3 and 11	None
	197	Compounds 11, 20 and 29	PAF1	Picoxystrobin	Picoxystrobin and Compound 30
	308	Compounds 20 and 29	n/a	Picoxystrobin, Compounds 2 and 11	n/a

Carrot root	30	Compounds 20 and 29, PYCR2 and PYCR3	Picoxystrobin and PAF1	Picoxystrobin and Compound 11	Compounds 2 and 7
	197	Picoxystrobin (10.7% TRRs, 0.021 ppm), PYCR2 and PYCR3 (15.1% TRRs, 0.030 ppm)	Picoxystrobin (28.8% TRRs, 0.010 ppm) and PAF1 (14.4% TRRs, 0.005 ppm)	Compounds 11, 20, 29 and 30	Compounds 8 and 30

Proposed metabolic scheme in rotational plants:



Picoxystrobin is extensively metabolized in soil mainly to Compounds 2, 3 and 8, which are then available to be taken up by the crops. In the crops, Compounds 2 and 3 conjugate to sugar moieties. Compounds 30 and 31, soil metabolites, were only observed in the confined accumulation study predominantly at the longer plant-back interval (197 DAT). The presence of radioactivity in glucose and other natural products in the wheat grain demonstrate that picoxystrobin is extensively degraded and enters the carbon pool of the plant as $^{14}CO_2$.

CROP FIELD TRIALS and Residue Decline on Field Corn and Sweet Corn	**PMRA# 1893780, 1893788**

A total of 15 trials including 2 decline trials were conducted in/on field corn (one trail in each of Zones 1, 2 and 6; 12 trials in Zone 5). At the test locations, picoxystrobin was applied three times as a foliar broadcast spray at the target rate of 0.2 lb a.i./A/application (equivalent to about 220 g a.i./ha/application) with the first treatment at growth stage R1 (silking). The last two applications were made at a 7 (±1) day interval with the last application at 7 days before the normal harvest. A non-ionic surfactant or crop oil concentrate (COC) was included in the spray mixture.

Corn forage was harvested 0 day after the third application, while corn grain and stover were harvested at a PHI of 7 days. For the decline sites, corn forage samples were harvested from the treatment plots immediately before the second application (-0 day) and then 0, 1, 3, and 6-7 days after the second application. Corn stover samples were harvested from the treatment plots immediately before the third application (-0 day) and then 0, 1, 3, and 7 days after the third application. Corn grain samples from two trials were also processed into corn aspirated grain fractions (AGF) according to the commercial practice.

The analysis results indicated that picoxystrobin residues declined in forage and stover samples with increasing PHIs from 0 to 7 days. The average processing factor for corn AGF based on samples from two trials was determined to be 14.3x.

A total of 11 trials including 2 decline trials were conducted in/on sweet corn (one trail in each of Zones 1, 2, 4, 7A, 10, 11 and 12; 4 trials in Zone 5). At the test locations, picoxystrobin was applied four times as a foliar broadcast spray at the target rate of 0.2 lb a.i./A/application (equivalent to about 220 g a.i./ha/application) with the first treatment targeted 28 days before normal harvest. The last three applications were made at 7-day intervals with the last application at 7 days before the normal harvest. A non-ionic surfactant was included in the spray mixture.

Sweet corn forage and ears were harvested at a PHI of 7 days. For the decline sites, corn forage samples were harvested from the treatment plots immediately before the last application (-0 day) and then 0, 1, 3, and 7 days after the last application.

The analysis results indicated that picoxystrobin residues declined in sweet corn forage samples with increasing PHIs from 0 to 7 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Picoxystrobin Residues* (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Field corn forage	639-676	0	13	0.83	8.1	8.1	3.3	3.9	1.8
Field corn stover		6-7	15	<0.013	6.6	6.6	1.9	2.1	1.8
Field corn grain			15	<0.01	<0.01	<0.01	<0.01	<0.01	0.0
Sweet corn forage	864-906	6-9	11	<0.01	2.2	2.2	0.53	0.74	0.69
Sweet corn K+CWHR			11	<0.01	<0.01	<0.01	<0.01	<0.01	0.0

* Averages of replicates of each trial are reported.

CROP FIELD TRIALS and Residue Decline on Wheat and Barley **PMRA# 1893782, 1893783, 1893784**

A total of 26 trials including 2 decline trials were conducted in/on wheat (One trail in each of Zones 2,4,6,7A, and 11; 4 trials in each of Zones 5and 8; 5 trials in Zone 7; 8 trials in Zone 14). A total of 21 trials were conducted in/on barley (One trail in each of Zones 1, 9, 10 and 11; 3 trials in Zone 5; 4 trials in Zone 7; 10 trials in Zone 14). At the test locations, picoxystrobin was applied as a foliar broadcast spray at the target rate of 0.2 lb a.i./A/application (equivalent to about 220 g a.i./ha/application) with the first treatment at a growth stage of Feekes 6 (BBCH-30), the second application at 14 days prior to Feekes 10.5 (BBCH-59), and the third application at Feekes 10.5 (BBCH-59). Wheat forage was harvested after the first application at a PHI of 7 days. The hay of wheat and barley was harvested after the third application at a PHI of 14 days. The straw and grain of wheat and barley was harvested at a PHI of 45 days after the third application. For most trials, a non-ionic surfactant was included in the spray mixture at 0.125% (v/v).

For the decline sites, wheat forage samples were harvested from the treatment plots immediately before the first application (-0 day) and then 0, 1, 3, 7, and 10 days after the first application. Wheat hay samples were harvested from the treatment plots immediately before the third application (-0 day) and then 0, 1, 3, 7, and 14 days after the third application. Wheat grain samples from two trials were also processed into wheat AGF according to the commercial practice.

The analysis results indicated that picoxystrobin residues declined in forage and hay samples with increasing PHIs from 0 to 14 days. The average processing factor for wheat AGF was determined as 18.6x.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Picoxystrobin Residues* (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Wheat forage	217-231	6-9	26	0.17	4.45	4.45	0.81	1.24	1.09
Wheat hay	655-685	14-17	26	0.14	3.05	3.05	0.73	1.26	1.3
Wheat straw		35-56	26	0.012	1.5	1.5	0.16	0.30	0.38
Wheat grain			26	<0.01	0.028	0.028	<0.01	<0.012	0.005
Barley Hay	655-693	9-17	21	0.16	3.65	3.65	0.63	1.01	0.95
Barley straw		44-77	21	0.027	0.74	0.74	0.15	0.19	0.20
Barley grain			21	<0.01	0.22	0.22	<0.016	<0.034	0.05

CROP FIELD TRIALS and Residue Decline on Soybean **PMRA# 1893789, 1893793**

A total of 21 trials including 2 decline trials were conducted in/on soybean (2 trials in Zone 2; 3 trials in Zone 4; 16 trials in Zone 5). At the test locations, picoxystrobin was applied three times as a foliar broadcast spray at the target rate of 0.2 lb a.i./A/application (equivalent to about 220 g a.i./ha/application) with the first treatment targeted at growth stage of R1. The last two applications were made at a 7 day interval with the last application at 14 days before the normal harvest. A non-ionic surfactant was included in the spray mixture.

Soybean forage and hay were harvested 14 days after the first application, while soybean seeds were harvested at a PHI of 14 days after the last application. For the decline sites, soybean forage and hay samples were harvested from the treatment plots at 0, 3, 7, 10 and 14 days after the first application. Soybean seed samples from two trials were also processed into soybean aspirated grain fractions (s) according to the commercial practice.
The analysis results indicated that picoxystrobin residues declined significantly in forage and hay samples with increasing PHIs from 0 to 14 days. The average processing factor for soybean AGF was determined as 255x.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Picoxystrobin Residues* (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Soybean forage	213-224	13-21	21	<0.01	0.76	0.76	0.20	0.25	0.17
Soybean hay			21	<0.01	1.9	1.9	0.8	0.78	0.52
Soybean seed	646-717	13-17	21	<0.01	0.039	0.039	<0.01	0.014	0.009

CROP FIELD TRIALS and Residue Decline on Canola **PMRA# 1893797**

A total of 18 trials including 2 decline trials were conducted in/on canola (one trail in each of Zones 2, 7 and &A; 2 trials in Zone 2; 3 trials in Zone 11; and 10 trials in Zone 14). At the test locations, picoxystrobin was applied two times as a foliar broadcast spray at the target rate of 0.2 lb a.i./A/application (equivalent to about 220 g a.i./ha/application) with 7 day intervals and the last application was targeted at 21 days before the normal harvest. A non-ionic surfactant was included in the spray mixture.

Mature canola seeds were harvested at a PHI of 21 days after the last application. For the decline sites, pod plus seed samples were harvested from the treatment plots immediately before the last application (-0 day) and then 0, 7 and 14 days after the last application. The seed samples from decline sites were harvested at 21 and 28 days after the last application.

The analysis results indicated that picoxystrobin residues declined significantly in canola pod plus seed samples with increasing PHIs from 0 to 14 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Picoxystrobin Residues* (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Canola seed	437-461	19-28	20	<0.01	0.047	0.047	0.02	0.023	0.013

CROP FIELD TRIALS and Residue Decline on Dried peas and beans **PMRA# 1893798**

A total of 11 trials including 2 decline trials were conducted in/on dried peas (one trial in Zone 5, 6 trials in Zone 11 and 4 trials in Zone 14). A total of 11 trials were conducted in/on dried beans (One trial in each of Zones 7A, 8 and 10; 6 trials in Zone 5; 2 trials in Zone 11). At the test locations, picoxystrobin was applied two times as a foliar broadcast spray at the target rate of 0.2 lb a.i./A/application (equivalent to about 220 g a.i./ha/application) with the second treatment targeted 14 days before normal harvest and an application interval of 7 days. A wide variety of different non-ionic surfactants, MSOs or COCs were included in the spray mixture.

Pea vines and hay were harvested at a PHI of 0 day after the last application, while pea and bean seeds were collected at a PHI of 14 days for all sites. The decline sites had two treatment plots, one for collection of pea forage and hay samples (TRT 2), and one for collection of pea seed samples (TRT 1). The first application was made earlier in TRT 2 than that in TRT 1. From TRT 2 plots, pea forage and hay samples were harvested immediately before the second treatment, and then 0, 3, 7, 10 and 14 days after the last treatment. From TRT 1 plot, pea seeds were harvested at a PHI of 14 days after the last treatment.

The analysis results indicated that picoxystrobin residues declined significantly in pea hay and vine with increasing PHIs from 0 to 14 days.

Commodity	Total Rate (g a.i./ha)	PHI (days)	Picoxystrobin Residues* (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	Std. Dev.
Pea Seed	433-455	13-14	11	<0.01	0.106	0.106	0.012	0.023	0.03
Pea Vine	448-455	0	6	3.35	9.35	9.35	5.98	6.02	2.5
Pea Hay			6	3.35	23	23	9.23	10.4	6.8
Bean Seed	430-451	14-15	11	<0.01	0.038	0.038	<0.01	0.016	0.01

* Averages of replicates of each trial are reported.

STORAGE STABILITY (RAC and the Processed Commodities)	**PMRA # 1893772, 1966871, 1968733**

Residues of picoxystrobin in barley samples (grain, forage and straw) from barley field trials that were stored for 22 months at <-18°C were re-analyzed. Residues of picoxystrobin obtained were compared to previously determined values in field trials. It was demonstrated that no significant decrease of picoxystrobin residues in barley matrices occurred for the frozen storage period of 22 months.

The interim frozen storage stability data for picoxystrobin and the metabolites Compound 2, Compound 3 and Compound 8 in crop samples (wheat forage, wheat straw, field corn grain, soybean seed, soybean meal, soybean oil, potato tuber, dry pea, lettuce, apple fruit, apple juice, apple pomace, and grape berries) for up to 12 months were provided.

Residues of picoxystrobin and metabolites (Compound 2, Compound 3 and Compound 8) were confirmed to be stable in wheat forage, wheat straw, field corn grain, soybean seed, soybean meal, soybean oil, potato tuber, dry pea, lettuce, apple fruit, apple juice, apple pomace, and grape berries for at least 12 months when stored at -20 ± 10ºC, except residues of metabolite IN-QDY63 in soybean oil, which were found to be stable for up to 6 months. This ongoing study will continue to 24 months and the final report will be submitted.

PROCESSED FOOD AND FEED - Corn	**PMRA# 1893800**

The results indicate that following a seasonal application rate of 3.3 kg a.i./ha (2.9 lb a.i./A), residues in/on field corn grain were 0.044-0.120 ppm for picoxystrobin, and below LOD (<0.003 ppm) for metabolites Compounds 2, 8 and 3. The following processing factors were determined.

Processed Commodity	Starch	Grits	Flour	Refined oil	Meal	Dry milled refined oil
Processing Factor	0.1x	0.4x	1.1x	6.8x	0.8x	4.4x

PROCESSED FOOD AND FEED - Soybean	**PMRA# 1893804**

The results indicate that following a seasonal application rate of 3.3 kg a.i./ha (2.9 lb a.i./A), residues in/on soybean seed were 0.032-0.29 ppm for picoxystrobin, <0.003-0.005 ppm for metabolite Compound 3, and below LOD (<0.003 ppm) for metabolites Compounds 2 and 8. The following processing factors were determined.

Processed Commodity	Hulls	Meal	Refined oil
Processing Factor	3.9x	0.2x	1.3x

PROCESSED FOOD AND FEED - Wheat	**PMRA# 1893801**

The results indicate that following a seasonal application rate of 3.4 kg a.i./ha (~3.0 lb a.i./A), residues in/on wheat grain were 0.014-0.058 ppm for picoxystrobin, 0.007 ppm for Compound 2, 0.003 ppm for Compound 8 and <0.003-0.005 ppm for Compound 3. The following processing factors were determined.

Processed Commodity	Bran	Flour	Middling	Shorts	Germ
Processing Factor	2.0x	0.2x	0.7x	1.0x	3.2x

PROCESSED FOOD AND FEED - Canola	**PMRA# 1893805**

The results indicate that following a seasonal application rate of 2.2 kg a.i./ha (1.9 lb a.i./A), residues in/on canola seed were 0.13-0.42 ppm for picoxystrobin and below LOD (<0.003 ppm) for metabolites Compounds 2, 3 and 8. The following processing factors were determined.

Processed Commodity	Presscake	Crude oil	Refined oil	Meal
Processing Factor	0.6x	2.1x	0.1x	0.4x

LIVESTOCK FEEDING – Dairy Cattle	**PMRA # 1893806, 1893807**

Lactating dairy cows were administered picoxystrobin at a target dose level of 40 ppm, 120 ppm and 400 ppm in the feeds for 29 consecutive days. A total of 14 cows were included in the study with 4 groups of lactating cows (2 cows for Group 1; 3 cows each for Groups 2 and 3; 6 cows in Group 4, three of which were used for the depuration phase). The dose levels of 40, 120, and 400 ppm represent 13x, 39x, and 130x, respectively, the estimated more balanced diet (MBD) to beef cattle and 2.9x, 8.6x, and 29x, respectively, the estimated more balanced diet to dairy cattle.

Commodity	**Feeding level (ppm)**	**Highest Residues (Picoxystrobin) (ppm)**	**MBD (ppm)**	**Anticipated Residue at MBD (ppm)**
			Beef/Dairy	
Whole milk	40	<0.01	3.09/14.00	<0.01
Skim milk		<0.01		<0.01
Cream		<0.01		<0.01
Fat		<0.01		<0.01
Liver		<0.01		<0.01
Kidney		<0.01		<0.01
Muscle		<0.01		<0.01

LIVESTOCK FEEDING – Laying Hens				PMRA # 1893808
Laying hens were administered picoxystrobin at a target dose level of 15 ppm, 45 ppm and 150 ppm in the feeds for 36 consecutive days. A total of 23 birds were included in the study with 4 groups of hens (10 hens per group in 3 subgroups of 3, 3 and 4 hens for Groups 1, 2 and 4; and 13 hens in 4 subgroups of 3, 3, 4 and 3 hens for Group 3). The dose levels of 15, 45, and 150 ppm represent 750x, 2250x, and 7500x, respectively, the estimated more balanced diet to poultry.				
Commodity	**Feeding level (ppm)**	**Highest Residues (Picoxystrobin) (ppm)**	**MBD (ppm)**	**Anticipated Residue at MBD (ppm)**
Whole Egg	15	<0.01	0.02	<0.01
Egg Yolk		<0.01		<0.01
Egg White		<0.01		<0.01
Fat		<0.01		<0.01
Liver		0.027		<0.01
Muscle		<0.01		<0.01
Proposed Maximum Residue Limits				
Commodity		Proposed MRL (ppm)		
Barley bran		0.5		
Barley		0.3		
Wheat germ		0.09		
Crop Subgroup 20A (Rapeseed Subgroup)		0.08		
Corn oil		0.07		
Crop Subgroup 6C (Dried Shelled Pea and Bean, except soybean)		0.06		
Wheat bran		0.06		
Dry soybeans		0.05		
Crop Group 15 (Cereal Grains, except barley and rice)		0.04		
Eggs		0.01		
Fat, meat and meat by-products of cattle, goats, hogs, horses, poultry, and sheep		0.01		
Milk		0.01		

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

PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT		Picoxystrobin	
RESIDUE DEFINITION FOR RISK ASSESSMENT			
METABOLIC PROFILE IN DIVERSE CROPS		The metabolic profile is similar in wheat, soybean, canola and apple	
ANIMAL STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT		Picoxystrobin	
RESIDUE DEFINITION FOR RISK ASSESSMENT			
METABOLIC PROFILE IN ANIMALS		The metabolic profile is similar in goat, hen and rats.	
FAT SOLUBLE RESIDUE		No	
DIETARY RISK FROM FOOD ONLY			
Basic chronic non-cancer dietary risk	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
ADI = 0.046 mg/kg bw/day	**All infants < 1 year**	0.8	2.0
	Children 1–2 years	1.9	2.4
EEC = 8.1 μg a.i./L, Level I	**Children 3 to 5 years**	1.6	2.1

	Children 6–12 years	1.1	1.4
	Youth 13–19 years	0.7	0.9
	Adults 20–49 years	0.6	0.9
	Adults 50+ years	0.4	0.8
	Females 13 to 49 yrs	0.5	0.8
	Total population	0.7	1.0
	POPULATION	**ESTIMATED RISK (95th Percentile) % of Acute Reference Dose (ARfD)**	
		Food Only	**Food and Water**
Basic Acute non-cancer dietary risk	**All infants < 1 year**	0.17	0.87
	Children 1–2 years	0.24	0.50
	Children 3 to 5 years	0.19	0.44
ARfD = 0.67 mg/kg bw/day	**Children 6–12 years**	0.14	0.31
	Youth 13–19 years	0.09	0.23
EEC = 27 μg a.i./L, Level I	**Adults 20–49 years**	0.09	0.26
	Adults 50+ years	0.06	0.21
	Females 13 to 49 yrs	0.07	0.24
	Total population	0.13	0.29

Table 7 Summary of DFR Values and Regression Analysis Results for Treated Soybean Foliage with Picoxystrobin

Input/Parameter	Pennsylvania	North Carolina	Michigan
Application Rate (kg a.i./ha) (Study Target Rate = 0.220 kg a.i./ha)	0.220	0.221	0.224
Spray Volume (LPH)	187	145	198
Measured Average Day 0 Residue ($\mu g/cm^2$)	0.221	0.216	0.136
Predicted Day 0 Residue ($\mu g/cm^2$)	0.340	0.421	0.158
Peak Residue ($\mu g/cm^2$)	0.221	0.315	0.208
Peak Residue % of application rate	10	14.3	9.3
Predicted dissipation rate (%)	48.1	32.9	28.7
Slope	-0.6554	-0.3983	-0.3421
Half-life (days)	1.1	1.7	2.0
R^2	0.97	0.75	0.88

Table 8 Fate and Behaviour in the Environment

Study	Test substance	Value[1]	Comments	Reference
Abiotic transformation				
Hydrolysis (25°C and 50°C)	picoxystrobin	half-life pH 5: stable pH 7: stable pH 9: stable (25°C); 16.6 d (50°C)	Not expected to be an important route of dissipation	1893544
Phototransformation on soil (20°C)	picoxystrobin	Half-life: 11.6 d (continuous irradiation); Predicted environmental half-life at 50°N: 16.4 d	Not expected to be an important route of dissipation (half-life >7 days)	1893546

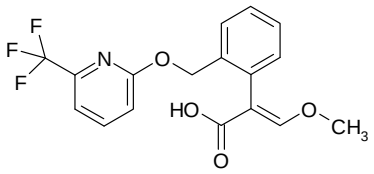
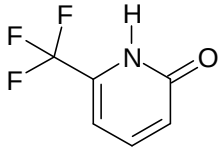
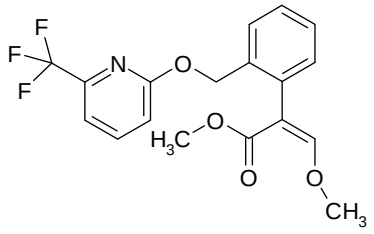
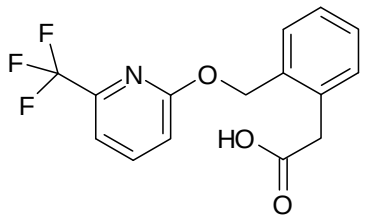
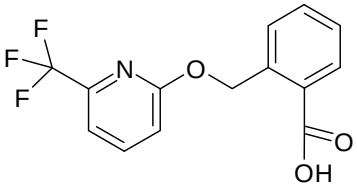
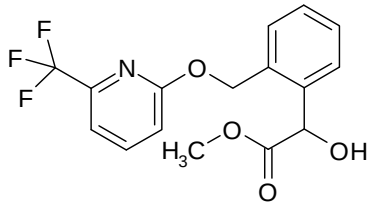
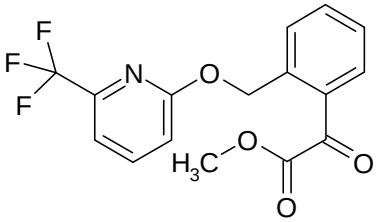
Study	Test substance	Value[1]		Comments	Reference
Phototransformation in water (25°C)	picoxystrobin	Half-life: 16 d (continuous irradiation); Predicted environmental half-life at 50°N: 25 d		Not expected to be an important route of dissipation (half-life >7 days)	1893545
Phototransformation in air	Picoxystrobin is not volatile under field conditions based on vapour pressure and Henry's law constant. A study is not required for picoxystrobin.				
Biotransformation					
Biotransformation in aerobic soil (20°C)	picoxystrobin	**Picoxystrobin (combined labels)**			1893547
		Hyde Farm sandy loam: DT_{50} = 31.4 d, DT_{90} = 104 d (SFO)		Slightly persistent	
		18 Acres clay loam: DT_{50} = 23.6 d, DT_{90} = 78.4 d (SFO)		Slightly persistent	
		Chamberlain's Farm sand: DT_{50} = 36.1 d, DT_{90} = 120 d (SFO)		Slightly persistent	
		Frensham sandy loam: DT_{50} = 28.4 d, DT_{90} = 94.3 d (SFO)		Slightly persistent	
		Compound 2 (combined labels) [2]			
		Hyde Farm sandy loam (day 50-119): DT_{50} = 51.5 d, DT_{90} = 171 d (SFO)		Moderately persistent	
		Chamberlain's Farm sand (day 50-119): DT_{50} = 50.5 d, DT_{90} = 168 d (SFO)		Moderately persistent	
		Frensham sandy loam (day 50-119): DT_{50} = 105 d, DT_{90} = 350 d (SFO)		Moderately persistent	
		Compound 3 (pyridinyl label) [2]			
		Hyde Farm sandy loam (day 50-364): DT_{50} = 105 d, DT_{90} = 348 d (SFO)		Moderately persistent	
		18 Acres clay loam (day 21-119): DT_{50} = 63.6 d, DT_{90} = 211 d (SFO)		Moderately persistent	
Biotransformation in anaerobic soil	Request for a waiver submitted and granted based on results of other studies.				1893550
Biotransformation in aerobic water-sediment systems (20°C)	picoxystrobin	Old Basing (sandy clay loam sediment)	Water: DT_{50} = 17.3 d, DT_{90} = 17.5 d (SFO)		1893549
			Sediment: DT_{50} = 36.5 d, DT_{90} = 121 d (SFO)		
			Total system: DT_{50} = 47.5 d, DT_{90} = 157 d (SFO)	Moderately persistent	
		Virginia Water (sand sediment)	Water: DT_{50} = 7.2 d, DT_{90} = 79.1 d (SFO)		
			Sediment: DT_{50} = 67.2 d, DT_{90} = 123 d (SFO)		
			Total system: DT_{50} = 57.3 d, DT_{90} = 190 d (SFO)	Moderately persistent	
Biotransformation in anaerobic water-sediment systems	picoxystrobin	purified water - UK sandy loam soil	Water: DT_{50} = 5.2 d, DT_{90} = 17.2 d (SFO)		1893548

Study	Test substance	Value[1]		Comments	Reference
(20°C)			Sediment: DT_{50} = 67.3 d, DT_{90} = 223 d (SFO)		
			Total system: DT_{50} = 54.2 d, DT_{90} = 180 d (SFO)	Moderately persistent	
Mobility					
Adsorption / desorption in soil	picoxystrobin	ERTC (sandy loam)	K_d = 5.1 mL/g; K_{OC} = 837 mL/g	Low mobility	1893551
		Champaign (silty clay loam)	K_d = 23.4 mL/g; K_{OC} = 1089 mL/g	Low mobility	
		Kenny Hill (sandy loam)	K_d = 22.2 mL/g; K_{OC} = 741 mL/g	Low mobility	
		18 Acres (sandy loam)	K_d = 16.5 mL/g; K_{OC} = 933 mL/g	Low mobility	
		Lilly Field (sand)	K_d = 3.5 mL/g; K_{OC} = 1067 mL/g	Low mobility	
		Hyde Farm (sandy clay loam)	K_d = 14.7 mL/g; K_{OC} = 878 mL/g	Low mobility	
Volatilization	picoxystrobin	Total [^{14}C]residue recoveries after 24 hours were 91.1% of the applied radioactivity soil and leaf systems.		Not volatile from soil and leaf surfaces	1893552
Bioconcentration/Bioaccumulation					
Bioconcentration in fish	picoxystrobin	BCF = 290 (whole fish) BCF = 1400 (viscera) BCF = 110 (flesh) BCF = 170 (carcass)		Low potential to bioconcentrate	1893461
Field studies					
Field dissipation in ecoregions representative of Canadian conditions	DPX-YT669 250SC (250 g a.i./L formulation)	Manitoba	Picoxystrobin (total soil profile) DT_{50} = 18.9 d, DT_{90} = 441 d (DFOP)	Slightly persistent	1893844
			Picoxystrobin (0-15 cm) DT_{50} = 17.3 d, DT_{90} = 434 d (DFOP)		
			Compound 2 DT_{50} = 148 d, DT_{90} = 492 d (SFO)[2]	Moderately persistent	
			Compound 3 DT_{50} = 227 d, DT_{90} = 753 d (SFO)[2]	Persistent	
			Compound 8 DT_{50} = 24.8 d, DT_{90} = 83.4 d (DFOP)[2]	Slightly persistent	
		Prince Edward Island	Picoxystrobin (total soil profile and 0-15 cm): DT_{50} = 1.8 d, DT_{90} = 76.9 d (DFOP)	Non-persistent	1893843
			Compound 2 DT_{50} = 59.2 d, DT_{90} =	Moderately persistent	

Study	Test substance	Value[1]		Comments	Reference
			197 d (SFO) [2]		
			Compound 3 DT_{50} = 36.4 d, DT_{90} = 121 d (SFO) [2]	Slightly persistent	
			Compound 8 DT_{50} = 24.9 d, DT_{90} = 82.6 d (SFO) [2]	Slightly persistent	
		Wisconsin	Picoxystrobin (total soil profile and 0-15 cm): DT_{50} = 2.8 d, DT_{90} = 71 d (DFOP)	Non-persistent	1893845
			Compound 2 DT_{50} = 34.3 d, DT_{90} = 114 d (SFO) [2]	Slightly persistent	
			Compound 3 DT_{50} = 214 d, DT_{90} = 710 d (SFO) [2]	Persistent	
			Compound 8 DT_{50} = 133 d, DT_{90} = 443 d (SFO) [2]	Moderately persistent	
Field dissipation in an ecoregions not representative of Canadian conditions (Supplemental studies)	DPX-YT669 250SC, YF10170, or YF10267 (250 g a.i./L formulations)	California, France, Germany, United Kingdom	Picoxystrobin DT_{50} = 2.7-37.2 d, DT_{90} = 73-351 d (IORE and DFOP)	Non-persistent to slightly persistent	1893832, 1893834, 1893836, 1893838, 1893840, 1893841, 1893842
			Compound 2 DT_{50} = 68 d, DT_{90} = 226 d (SFO) [2]	Moderately persistent	
			Compound 3 DT_{50} = 10.8-59 d, DT_{90} = not-calculated-36 d (SFO and ln linear regression) [2]	Non-persistent to moderately persistent	
			Compound 8 DT_{50} = 12.5-172 d, DT_{90} = 42-572 d (SFO and ln linear regression) [2]	Non-persistent to moderately persistent	
Field dissipation – outdoor pond study	YF10267 (250 g a.i./L formulation)	Berkshire, UK	Total system DT_{50} = 35.5 d, DT_{90} = 118 d (calculated by the study authors)	Slightly persistent	1893550

[1] Kinetics models: DFOP = Double first-order in parallel; SFO = single first-order; IORE = indeterminate order rate equation.
[2] Half-lives/DT_{50}s and DT_{90}s for transformation products incorporate both formation and decline.

Table 9 Name and chemical structure of environmental transformation products of picoxystrobin

Code Name/ Synonym	Chemical Name	Chemical Structure
Compound 2; ZA1963/02; IN-QDY62; R403092	(E)-2-{2-[6-(trifluoromethyl)pyridin-2-yloxymethyl]phenyl}-3-methoxyacrylic acid	
Compound 3; ZA1963/03; IN-QDK50; R403814	6-(Trifluoromethyl)pyridin-2H-2-one	
Compound 4; ZA1963/04	Methyl (Z)-2-{2-[6-(trifluoromethyl)pyridin-2-yloxymethyl]phenyl}-3-methoxyacrylate	
Compound 7; ZA1963/07; IN-QFA35; R408631	2-{2-[6-(trifluoromethyl)pyridin-2-yloxymethyl]phenyl}acetic acid	
Compound 8; ZA1963/08; IN-QDY63; R408509	2-[6-(Trifluoromethyl)pyridin-2-yloxymethyl]-benzoic acid	
Compound 12; ZA1963/12	Methyl 2-hydroxy-{2-[6-(trifluoromethyl)pyridin-2-yloxymethyl]phenyl}-acetate	
Compound 13; ZA1963/13	Methyl 2-oxo-{2-[6-(trifluoromethyl)pyridin-2-yloxymethyl]phenyl}-acetate	

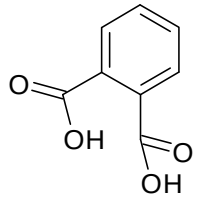
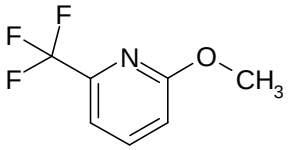
Code Name/ Synonym	Chemical Name	Chemical Structure
ZA1963/15; Compound 15	Phthalic acid	
Compound 26; IN-QDY64; R413834	2-Methoxy-6-(trifluoromethyl)pyridine	
Carbon dioxide	Carbon dioxide	O=C=O

Table 10 Summary of formation of transformation products (% applied radioactivity) formed in environmental studies with picoxystrobin

Study type				Maximum % AR[1] (day)	Final %AR[1] (study length)	Reference
Compound 2						
Hydrolysis	pH 9 (50ºC)			**32.1** (32)	**32.1** (32)	1893544
Soil photolysis				Not identified but not major		1893546
Aqueous photolysis				Not identified but not major		1893545
Aerobic soil	Sandy loam (Hyde Farm)	Pyridinyl label		**16.8** (50)	1.5 (364)	1893547
		Phenylacrylate label		**18.7** (29)	1.9 (364)	
	Sandy clay loam	Pyridinyl label		9.4 (9)	4.0 (119)	
		Phenylacrylate label		9.1 (9)	2.7 (119)	
	Sand	Pyridinyl label		**14.9** (50)	4.5 (119)	
		Phenylacrylate label		**17.3** (29)	3.7 (119)	
	Sandy loam (Frensham)	Pyridinyl label		**26.1** (50)	**17.3** (119)	
		Phenylacrylate label		**26.3** (29)	**13.5** (119)	
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment	Old Basing	Pyridinyl label	Water	**37.4** (120)	**37.4** (120)	1893549
			Sediment	**29.8** (120)	**29.8** (120)	
			System	**67.2** (120)	**67.2** (120)	
		Phenylacrylate label	Water	**38.2** (120)	**38.2** (120	
			Sediment	**30.7** (120)	**30.7** (120)	
			System	**68.9** (120)	**68.9** (120)	
	Virginia Water	Pyridinyl label	Water	**16.6** (83)	6.3 (120)	
			Sediment	6.7 (51)	1.1 (120)	
			System	**22.5** (51)	7.4 (120)	
		Phenylacrylate label	Water	**16.4** (83)	6.0 (120)	
			Sediment	7.6 (51)	1.0 (120)	
			System	**20.6** (51)	7.0 (120)	
Anaerobic water-sediment	Purified water-UK sandy loam soil	Pyridinyl label	Water	**40.0** (360)	**40.0** (360)	1893548
			Sediment	**33.3** (360)	**33.3** (360)	
			System	**73.2** (360)	**73.2** (360)	
		Phenylacrylate	Water	**37.0** (360)	**37.0** (360)	

Study type				Maximum % AR[1] (day)	Final %AR[1] (study length)	Reference
		label	Sediment	**35.9** (220)	**30.4** (360)	
			System	**69.4** (220)	**67.4** (360)	
Field studies	Terrestrial	Manitoba		3% i.m.p.[2] (95)	0.3% i.m.p. (447)	1893844
		Prince Edward Island		Max average 9.2% i.m.p. (43); max replicate: **12.5%** i.m.p. (43)	Not analyzed (372)	1893843
		Wisconsin		7.4% i.m.p. (48)	na (357)	1893845
		California		2.9% i.m.p. (43)	na (363)	1893842
		France 1996/1997	Site 1	1.8% i.m.p. (15, 62)	<1.8% i.m.p. (367)	1893832
			Site 2	6.4% i.m.p. (27-365)	6.4% i.m.p. (365)	1893832
		UK 1996/1997		4.6% i.m.p. (364)	4.6% i.m.p. (364)	1893841
		Germany 1996/1997		4% i.m.p. (96)	<0.9% i.m.p. (365)	1893834
		France (1997/1998)	Site 1	<1.5% i.m.p.	<1.5% i.m.p. (365)	1893838
			Site 2	<2.6% i.m.p.	<2.6% i.m.p. (361)	1893838
		Germany 1997/1998		<2.1% i.m.p.	<2.1% i.m.p. (391)	1893836
		UK 1997/1998		1.4% i.m.p. (56, 96, 284)	<1.4% i.m.p. (379)	1893840
Compound 3						
Hydrolysis				Not identified but not major		1893544
Soil photolysis		Pyridinyl label		**28.3** (3.8)	**13.1** (19.8)	1893546
Aqueous photolysis		Pyridinyl label		1.9 (17.9)	1.9 (17.9)	1893545
Aerobic soil	Sandy loam (Hyde Farm)	Pyridinyl label		**13.8** (50)	0.7 (364)	1893547
	Sandy clay loam	Pyridinyl label		**13.7** (21)	3.9 (119)	
	Sand	Pyridinyl label		9.4 (50)	5.8 (119)	
	Sandy loam (Frensham)	Pyridinyl label		**10.3** (50)	7.9 (119)	
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment	Old Basing	Pyridinyl label	Water	1.0 (83)	0.9 (120)	1893549
			Sediment	1.1 (120)	1.1 (120)	
			System	2.0 (120)	2.0 (120)	
	Virginia Water	Pyridinyl label	Water	4.5 (120)	4.5 (120)	
			Sediment	1.5 (120)	1.5 (120)	
			System	6.0 (120)	6.0 (120)	
Anaerobic water-sediment	Purified water-UK sandy loam soil	Pyridinyl label	Water	0.8 (360)	0.8 (360)	1893548
			Sediment	0.6 (360)	0.6 (360)	
			System	1.5 (360)	1.5 (360)	
Field studies	Terrestrial	Manitoba		6.7% i.m.p. (29)	0.7% i.m.p. (447)	1893844
		Prince Edward Island		3.1% i.m.p. (30)	Not analyzed (372)	1893843
		Wisconsin		2.5% i.m.p. (16)	Not analyzed (357)	1893845
		California		5.1% i.m.p. (11)	Not analyzed (363)	1893842
		France 1996/1997	Site 1	3.4% i.m.p. (15, 28)	<0.8% i.m.p. (367)	1893832
			Site 2	4.4% i.m.p. (98)	<1.5% i.m.p. (365)	1893832

Study type				Maximum % AR[1] (day)	Final %AR[1] (study length)	Reference
		UK 1996/1997		2.1% i.m.p. (94)	1.4% i.m.p. (364)	1893841
		Germany 1996/1997		1.9% i.m.p. (4-28)	<2% i.m.p. (365)	1893834
		France (1997/1998)	Site 1	1.4% i.m.p. (14, 28)	<0.7% i.m.p. (365)	1893838
			Site 2	2.4% i.m.p. (13)	<1.2% i.m.p. (361)	1893838
		Germany 1997/1998		1.9% i.m.p. (7-27)	<1% i.m.p. (391)	1893836
		UK 1997/1998		3.2% i.m.p. (7)	<0.6% i.m.p. (379)	1893840
Compound 4						
Hydrolysis				Not identified but not major		1893544
Soil photolysis		Pyridinyl label		2.5 (0.8)	1.1 (19.8)	1893546
		Phenylacrylate label		3.8 (3.8)	2.2 (20.7)	
Aqueous photolysis		Pyridinyl label		**14.2** (3.7)	8.3 (17.9)	1893545
		Phenylacrylate label		**11.7** (3.7)	9.1(17.7)	
Aerobic soil				Not identified but not major		1893547
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment				Not identified but not major		1893549
Anaerobic water-sediment				Not identified but not major		1893548
Field studies				Not analyzed		
Compound 7						
Hydrolysis	pH 9 (50ºC)			**37.9** (32)	**37.9** (32)	1893544
Soil photolysis				Not identified but not major		1893546
Aqueous photolysis				Not identified but not major		1893545
Aerobic soil				Likely present at minor concentrations		1893547
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment	Old Basing	Pyridinyl label	Water	2.3 (30)	0.2 (120)	1893549
			Sediment	1.4 (120)	1.4 (120)	
			System	1.6 (120)	1.6 (120)	
		Phenylacrylate label	Water	0.4 (83)	0.2 (120)	
			Sediment	2.9 (120)	2.9 (120)	
			System	3.1 (120)	3.1 (120)	
	Virginia Water	Pyridinyl label	Water	**25.9** (120)	**25.9** (120)	
			Sediment	**12.8** (83)	**12.4** (120)	
			System	**38.3** (120)	**38.3** (120)	
		Phenylacrylate label	Water	**24.2** (120)	**24.2** (120)	
			Sediment	**14.2** (83)	**12.2** (120)	
			System	**36.4** (120)	**36.4** (120)	
Anaerobic water-sediment	Purified water-UK sandy loam soil	Pyridinyl label	Water	<0.05 (0-360)	<0.05 (0-360)	1893548
			Sediment	1.8 (360)	1.8 (360)	
			System	1.8 (360)	1.8 (360)	
		Phenylacrylate label	Water	<0.05 (0-360)	<0.05 (360)	
			Sediment	1.6 (360)	1.6 (360)	
			System	1.6 (360)	1.6 (360)	
Field studies				Not analyzed		
Compound 8						
Hydrolysis	pH 9 (50ºC)			Not identified but not major		1893544
Soil photolysis		Pyridinyl label		2.4 (0.8)	2.3 (19.8)	1893546
		Phenylacrylate label		3.0 (6.9-13.7)	2.9 (20.7)	
Aqueous photolysis				Not identified but not major		1893545

Study type				Maximum % AR[1] (day)	Final %AR[1] (study length)	Reference
Aerobic soil				Likely present at minor concentrations		1893547
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment	Old Basing	Pyridinyl label	Water	2.7 (120)	2.7 (120)	1893549
			Sediment	0.6 (83)	0.2 (120)	
			System	2.9 (120)	2.9 (120)	
		Phenylacrylate label	Water	1.1 (83)	0.9 (120)	
			Sediment	0.8 (83)	Not detected (120)	
			System	1.9 (83)	0.9 (120)	
	Virginia Water	Pyridinyl label	Water	8.4 (120)	8.4 (120)	
			Sediment	2.7 (120)	2.7 (120)	
			System	**11.1** (120)	**11.1** (120)	
		Phenylacrylate label	Water	8.5 (120)	8.5 (120)	
			Sediment	2.9 (120)	2.9 (120)	
			System	**11.4** (120)	**11.4** (120)	
Anaerobic water-sediment	Purified water-UK sandy loam soil	Pyridinyl label	Water	0.4 (220)	<0.05 (360)	1893548
			Sediment	0.7 (120)	0.3 (360)	
			System	0.7 (120)	0.3 (360)	
		Phenylacrylate label	Water	<0.05 (0-360)	<0.05 (360)	
			Sediment	0.4 (91)	<0.05 (360)	
			System	0.4 (91)	<0.05 (360)	
Field studies	Terrestrial	Manitoba		5.1% i.m.p. (95)	0.4% i.m.p. (447)	1893844
		Prince Edward Island		**12.5%** i.m.p. (30)	Not analyzed (372)	1893843
		Wisconsin		7.2% i.m.p. (30)	Not analyzed (357)	1893845
		California		**12.6**% i.m.p. (11)	Not analyzed (363)	1893842
		France 1996/1997	Site 1	**13.7**% i.m.p. (7, 28)	<1.5% i.m.p. (367)	1893832
			Site 2	**16.2**% i.m.p. (14)	<2.7% i.m.p. (365)	1893832
		UK 1996/1997		**10.3**% i.m.p. (28)	2.6% i.m.p. (364)	1893841
		Germany 1996/1997		5.1% i.m.p. (28, 63)	<1.7% i.m.p. (365)	1893834
		France (1997/1998)	Site 1	3.8% i.m.p. (6, 14)	<1.3% i.m.p. (365)	1893838
			Site 2	**15.3**% i.m.p. (13)	<2.2% i.m.p. (361)	1893838
		Germany 1997/1998		**12.3**% i.m.p. (14)	<1.8% i.m.p. (391)	1893836
		UK 1997/1998		7.0% i.m.p. (28, 56)	<1.2% i.m.p. (379)	1893840
Compound 12						
Hydrolysis				Not identified but not major		1893544
Soil photolysis		Pyridinyl label		1.4 (3.8)	0.9 (19.8)	1893546
		Phenylacrylate label		2.3 (6.9, 20.7)	2.3 (20.7)	
Aqueous photolysis		Pyridinyl label		**15.3** (17.9)	**15.3** (17.9)	1893545
		Phenylacrylate label		**14.5** (17.7)	**14.5** (17.7)	
Aerobic soil				Not identified but not major		1893547
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment				Not identified but not major		1893549
Anaerobic water-sediment				Not identified but not major		1893548
Field studies				Not analyzed		

Study type				Maximum % AR[1] (day)	Final %AR[1] (study length)	Reference
Compound 13						
Hydrolysis				Not identified but not major		1893544
Soil photolysis		Pyridinyl label		2.0 (0.8)	0.9 (19.8)	1893546
		Phenylacrylate label		2.1 (0.7-3.8)	1.2 (20.7)	
Aqueous photolysis				Not identified but not major		1893545
Aerobic soil				Not identified but not major		1893547
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment				Not identified but not major		1893549
Anaerobic water-sediment				Not identified but not major		1893548
Field studies				Not analyzed		
Compound 15						
Hydrolysis				Not identified but not major		1893544
Soil photolysis		Phenylacrylate label		5.8 (13.7)	5.2 (20.7)	1893546
Aqueous photolysis				Not identified but not major		1893545
Aerobic soil				Not identified but not major		1893547
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment				Not identified but not major		1893549
Anaerobic water-sediment				Not identified but not major		1893548
Field studies				Not analyzed		
Compound 26						
Hydrolysis				Not identified but not major		1893544
Soil photolysis		Pyridinyl label		Not identified but not major		1893546
Aqueous photolysis		Pyridinyl label		Not identified but not major		1893545
Aerobic soil	Sandy loam (Hyde Farm)	Pyridinyl label		6.9 (364) [3]	6.9 (364) [3]	1893547
				12.9 (115) [4] (modified trapping system)	**12.9** (115) [4] (modified trapping system)	
	Sandy clay loam	Pyridinyl label		8.2 (119) [3]	8.2 (119) [3]	
				22.8 (115) [4] (modified trapping system)	**22.8** (115) [4] (modified trapping system)	
	Sand	Pyridinyl label		8.2 (119) [3]	8.2 (119) [3]	
	Sandy loam (Frensham)	Pyridinyl label		5.7 (119) [3]	5.7 (119) [3]	
	Sandy clay loam	Pyridinyl label		**31.2** (119) [4]	**31.2** (119) [4]	1966852
Aerobic soil (sealed biometer flask)	Sandy loam	Pyridinyl label	Soil	**10.1** (84) [4,5]	4.8 (119) [4,5]	1966846
			Aerial component	5.4 (84) [4,5]	1.0 (119) [4,5]	
Anaerobic soil				Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment				Not identified but not major		1893549
Anaerobic water-sediment				Not identified but not major		1893548
Field studies				Not analyzed		
Carbon dioxide						
Hydrolysis				Not analyzed		1893544
Soil photolysis		Pyridinyl label		**32.2** (19.8)	**32.2** (19.8)	1893546
		Phenylacrylate label		**22.0** (20.7)	**22.0** (20.7)	

Study type			Maximum % AR[1] (day)	Final %AR[1] (study length)	Reference
Aqueous photolysis		Pyridinyl label	6.4 (17.9)	6.4 (17.9)	1893545
		Phenylacrylate label	2.5 (17.7)	2.5 (17.7)	
Aerobic soil	Sandy loam (Hyde Farm)	Pyridinyl label	**33.9** (364)	**33.9** (364)	1893547
		Phenylacrylate label	**59.9** (364)	**59.9** (364)	
	Sandy clay loam	Pyridinyl label	**32.5** (119)	**32.5** (119)	
		Phenylacrylate label	**40.1** (119)	**40.1** (119)	
	Sand	Pyridinyl label	**22.8** (119)	**22.8** (119)	
		Phenylacrylate label	**33.6** (119)	**33.6** (119)	
	Sandy loam (Frensham)	Pyridinyl label	**20.1** (119)	**20.1** (119)	
		Phenylacrylate label	**29.9** (119)	**29.9** (119)	
Anaerobic soil			Waiver requested and granted based on results of other studies.		1893550
Aerobic water-sediment	Old Basing	Pyridinyl label	2.9 (120)	2.9 (120)	1893549
		Phenylacrylate label	2.9 (120)	2.9 (120)	
	Virginia Water	Pyridinyl label	5.8 (120)	5.8 (120)	
		Phenylacrylate label	6.1 (120)	6.1 (120)	
Anaerobic water-sediment	Purified water-UK sandy loam soil	Pyridinyl label	0.7 (360)	0.7 (360)	1893548
		Phenylacrylate label	0.2 (360)	0.2 (360)	
Field studies			Not analyzed		

[1] AR = applied radioactivity
[2] i.m.p. = initial measured parent.
[3] Difficulties in trapping the volatile transformation product, Compound 26, made accurate quantification problematic. Actual concentrations may be significantly higher than those measured.
[4] Supplemental study.
[5] Given that the radioactive recovery was poor at key sampling periods in the study, there is a significant amount of uncertainty with some of the reported concentrations.

Table 11 Toxicity of picoxystrobin, a 250 g a.i./L Soluble Concentrate formulation and major transformation products to non-target terrestrial species.

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
Invertebrates					
Earthworm (*Eisenia foetida*)	14-d Acute	Picoxystrobin	LC_{50}: 6.7 mg a.i./kg soil; NOEC (mortality and weight loss): 3.2 mg a.i./kg soil	No classification	1893484
	14-d Acute	AB12796B (250 g a.i./L SC formulation)	LC_{50}: 4.0 mg a.i./kg soil; NOEC (mortality): 3.2 mg a.i./kg soil; NOEC (weight loss): 2.1 mg a.i./kg soil	No classification	1893827
	14-d Acute, effects of aging and soil moisture	AB12796B (250 g a.i./L SC formulation)	>67% mortality observed at concentrations of 4 mg a.i./kg soil and higher, under all moisture levels (25-50%) and	No classification	

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
			soil age (0-14 days) combinations tested. Mortality increased with soil moisture Mortality appeared to be higher in soils with residues 0-4 days old compared to those with residues 7-14 days old.		
	14-d Acute	R403092/ Compound 2	LC_{50}: >1000 mg/kg soil; NOEC (mortality): 1000 mg/kg soil; NOEC (weight loss): 100 mg/kg soil	No classification	1893485
	14-d Acute	R403814/ Compound 3	LC_{50}: 320 mg/kg soil; NOEC (mortality and weight change): 100 mg/kg soil	No classification	1893488
	14-d Acute	R408509/ Compound 8	LC_{50}: 320 mg/kg soil; NOEC (mortality and weight change): 100 mg/kg soil	No classification	1893486
	8-wk Chronic	A12796B (250 g a.i./L SC formulation)	Adult survival: 4-wk LC_{50}: >5 mg a.i./kg soil; 4-wk NOEC: 2.5 mg a.i./kg soil Adut Biomass: 4-wk NOEC: 5 mg a.i./kg soil Number of Juveniles: 8-wk EC_{50}: 2.55 mg a.i./kg soil; 8-wk NOEC: 0.63 mg a.i./kg soil	No classification	1893829
Earthworms (naturally occurring populations)	380-d field study; spring barley field in North East Germany 1 application at 0 (control), 62.5, 125, 250 and 500 g a.i./ha	A12796B (250 g a.i./L SC formulation)	No significant effect on total abundance or total biomass of earthworms observed after 380 days.	No classification	1893530
	381-d field study; spring barley field in	A12796B (250 g a.i./L SC formulation)	At 500 g a.i./ha, total abundance and total biomass of	No classification	1893531

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
	North Germany 1 application at 0 (control), 62.5, 125, 250 and 500 g a.i./ha		earthworms were reduced by 39% and 42%, respectively, after 381 days. Juveniles were more sensitive than adult worms.		
	396-d field study; nine wheat or barley plots in Northern France 2 applications at 0 (control), 125 and 250 g a.i./ha, at a 21-d interval	A12796B (250 g a.i./L SC formulation)	No significant effect on total abundance or biomass of earthworms observed at any site by 12 months after application.	No classification	1893508
	12-month field study; spring barley field in the Southern UK 1 application at 0 (control), 62.5, 125, 250 and 500 g a.i./ha	A12796B (250 g a.i./L SC formulation)	No significant effect on abundance or biomass of any taxonomic or ecological group apparent by seven months after application.	No classification	1893529
	12-month field study; bare ground plot in the UK 2 applications at 0 (control), 50, 125 and 250 g a.i./ha, at a 14-d interval	ZA1963 25SC (250 g a.i./L SC formulation)	No adverse effect on abundance or weight of earthworms immediately after and up to 12 months after application.	No classification	1893535
	374-d field study; winter wheat field in Sweden 1 application at 0 (control), 62.5, 125, 250 and 500 g a.i./ha	Acanto 250 SC (A-12796B) (250 g a.i./L SC formulation)	31-d EC_{50} (worm numbers): 168.5 g a.i./ha; 31-d NOEC (worm numbers): <62.5 g a.i./ha Reduced number of worms 374 days after application at 500 g a.i./ha, likely due to a slight reduction the number of juveniles. No significant effect on abundance or biomass by 374 days after application at	No classification	1893533

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
			rates up to and including 250 g a.i./ha.		
	21-d field study; 99 wheat or barley fields in France, the UK and Germany 2 applications at 0 (control), 75, 125, 175 and 250 g a.i./ha at a 21-d interval (also 200 g a.i./ha mixed with 360 g fenpropidin and 100 g a.i./ha propiconazole in Germany only)	Acanto 250 SC (A-12796B) (250 g a.i./L SC formulation)	Unacceptable study	No classification	1893490
Honey bee (*Apis mellifera*)	48-h Oral	Picoxystrobin	Not tested due to low solubility in water	Not tested	1893541
	48-h Contact	Picoxystrobin	LD_{50}: >200 µg a.i./bee; NOEL: 200 µg a.i./bee	Relatively non-toxic	1893541
	48-h Oral	YF10267 (250 g a.i./L SC formulation)	LD_{50}: >200 µg a.i./bee; NOEL: 200 µg a.i./bee	Relatively non-toxic	1893540
	48-h Contact	YF10267 (250 g a.i./L SC formulation)	LD_{50}: >200 µg a.i./bee; NOEL: 200 µg a.i./bee	Relatively non-toxic	1893540
Predatory mite (*Typhlodromus pyri*)	7-d Contact, Glass plates (screening level)	YF10267 (250 g a.i./L SC formulation)	Corrected mortality at 7 days was 55.6% at 250 g a.i./ha and 49.4% at 500 g a.i./ha	No classification	1893539
Green lacewing (*Chrysoperla carnea*)	65-d Semi-field (mortality: 7-d; fecundity: 48-h)	YF10267 (250 g a.i./L SC formulation)	No significant effects on mortality and fecundity after one or two applications at 250 g a.i./ha at a 13-day interval.	No classification	1893538
Parasitic wasp (*Aphidius rhopalosiphi*)	48-h Contact, Leaf substrate (extended laboratory)	YF10267 (250 g a.i./L SC formulation)	Corrected mortality at 48 hours was 100% at both 250 and 500 g a.i/ha.	No classification	1893536
	12-d Aged residue	YF10267 (250 g a.i./L SC formulation)	Day 0 corrected mortality was 65.2% and 74.4% after one and two applications at 250 g a.i./ha, respectively. No significant effects on mortality and fecundity after 3 days.	No classification	1893537

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
Birds					
Bobwhite quail (*Colinus virginianus*)	Acute	Picoxystrobin	LD_{50}: >2250 mg a.i./kg bw; NOEL: 2250 mg a.i./kg bw	Practically non-toxic	1893465
	5-d Dietary	Picoxystrobin	LC_{50}>5200 mg a.i./kg diet; NOEC: 5200 mg a.i./kg diet LD_{50} >1830 mg a.i./kg bw/d (reviewer-calculated)	Practically non-toxic	1893469
	20-wk Reproduction	Picoxystrobin	NOEC: 1190 mg a.i./kg diet (mean measured; highest concentrationt tested) Daily dose: 110.3 mg a.i./kg bw/d (reviewer-calculated)	No classification	1893478
Mallard duck (*Anas platyrhynchos*)	5-d Dietary	Picoxystrobin	LC_{50} >5200 mg a.i./kg diet; NOEC: 5200 mg a.i./kg diet LD_{50} >2298 mg a.i./kg bw/d (reviewer-calculated)	Practically non-toxic	1893471
	21-wk Reproduction	Picoxystrobin	NOEC: 1350 mg a.i./kg diet (highest concentration tested) Daily dose: 178 mg a.i./kg bw/d (reviewer-calculated)	No classification	1893483
Zebra finch (*Taeniopygia guttata*)	Acute	Picoxystrobin	LD_{50} >486 mg a.i./kg bw; NOEL: 486 mg a.i./kg bw	No mortality was observed at 486 mg a.i./kg bw	1893467
Mammals					
Rat	Acute	Picoxystrobin	LD_{50} >5000 mg a.i./kg bw	Practically non-toxic	1893595
	Acute	250 g a.i./L SC formulation	LD_{50} >2000 mg EP/kg bw/d (equivalent to >460 mg a.i./kg bw/d)	Formulation is practically non-toxic	1893818
	4-h Acute inhalation	R413834/ Compound 26	LC_{50} >3629 ppm (26.24 mg/L) for males; LC_{50} >1450 ppm (10.48 mg/L) for females	No classification	1966847
	11-wk Reproduction	Picoxystrobin	Parental and Offspring NOAEL: 55.5 mg/kg bw/d; LOAEL: 137.5 mg/kg bw/d (Parental effects: reductions in body weight, body	No classification	1893649

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
			weight gain, and food consumption. Offspring effects: reductions in body weight in F_1 and F_2 rats) Reproduction NOAEL: 137.5 mg/kg bw/d (highest dose tested)		
	10-wk Reproduction	Picoxystrobin	Parental NOAEL: 5.4 mg/kg bw/d; LOAEL: 21.5 mg/kg bw/d (reduced body weight, body weight gain, and food consumption) Offspring NOAEL: 21.5 mg/kg bw/d; LOAEL: 80 mg/kg bw/d (reductions in body weights in F_1 rats at post natal day 29, and in F_2 rats at post natal days 22 and 29). Reproduction NOAEL: 80 mg/kg bw/d (highest dose tested)	No classification	1893638
Terrestrial vascular plants					
Corn (*Zea mays*), oat (*Avena sativa*), onion (*Allium cepa*), ryegrass (*Lolium perenne*), cucumber (*Cucumis sativa*), oilseed rape (*Brassica napus*), pea (*Pisum sativum*), soybean (*Glycine max*), sugar beet (*Beta vulgaris*), and tomato (*Lycopersicon esculentum*)	21-d Seedling emergence	250 g a.i./L SC formulation	ER_{25} >500 g a.i./ha (all tested species) ER_{50} >500 g a.i./ha (all tested species)	No classification	1893560
	21-d Vegetative vigour	250 g a.i./L SC formulation	ER_{25} >500 g a.i./ha (all tested specied) ER_{50} >500 g a.i./ha (all tested species)	No classification	1893561

[1] Atkins et al.(1981) for bees and US EPA classification for others, where applicable

Table 12 Screening level risk assessment for picoxystrobin and transformation products on non-target terrestrial species, other than birds and mammals

Organism	Exposure	Endpoint value	EEC[1]	RQ	Level of Concern
Invertebrates					
Earthworm (*Eisenia foetida*)	Acute, picosystrobin formulation	$LC_{50}/2$ = 2 mg a.i./kg soil (study with the formulation)	0.27 mg a.i./kg soil (sweet corn use)	0.1	Not exceeded
	Chronic, picoxystrobin	NOEC = 0.63 mg a.i./kg soil	0.27 mg a.i./kg soil (sweet corn use)	0.4	Not exceeded
	Acute, Compound 2	$LC_{50}/2$ >500 mg/kg soil	0.26 mg/kg soil (sweet corn use)	<0.0005	Not exceeded
	Acute, Compound 3	$LC_{50}/2$ = 160 mg/kg soil	0.12 mg/kg soil (sweet corn use)	0.0008	Not exceeded
	Acute, Compound 8	$LC_{50}/2$ = 160 mg/kg soil	0.22 mg/kg soil (sweet corn use)	0.001	Not exceeded
Honey bee (*Apis mellifera*)	Oral	LR_{50} >224 kg a.i./ha[2]	0.399 kg a.i./ha (sweet corn use)	<0.002	Not exceeded
	Contact	LR_{50} >224 kg a.i./ha[2]	0.399 kg a.i./ha (sweet corn use)	<0.002	Not exceeded
Predatory mite (*Typhlodromus pyri*)	Contact, glass plate	LR_{50} <250 g a.i./ha; corrected mortality at 7-days was 55.6% at 250 g a.i./ha and 49.4% at 500 g a.i./ha	Sweet corn use: In field: 399 g a.i./ha Off-field (aerial appl., 23% drift): 92 g a.i./ha Off-field (ground appl., 6% drift): 24 g a.i./ha	>1.6 >0.4 >0.1	Possibly exceeded (LOC≥2)[3]
			Dry legume use: In field: 303 g a.i./ha Off-field (aerial appl., 23% drift): 70 g a.i./ha Off-field (ground appl., 6% drift): 18 g a.i./ha	>1.2 >0.3 >0.07	
Parasitic wasp (*Aphidius rhopalosiphi*)	Contact, leaf substrate	LR_{50} <250 g a.i./ha; corrected mortality at 48 hours was 100% at both 250 and 500 g a.i/ha	Sweet corn use: In field: 399 g a.i./ha Off-field (aerial appl., 23% drift): 92 g a.i./ha Off-field (ground appl., 6% drift): 24 g a.i./ha	>1.6 >0.4 >0.1	Exceeded Possibly exceeded Possibly exceeded
			Dry legume use: In field: 303 g a.i./ha Off-field (aerial appl., 23% drift): 70 g a.i./ha	>1.2 >0.3	Exceeded Possibly exceeded

Organism	Exposure	Endpoint value	EEC[1]	RQ	Level of Concern
			Off-field (ground appl., 6% drift): 18 g a.i./ha	>0.07	Possibly exceeded
	Aged residue	LR_{50} <250 g a.i./ha; corrected mortality was 65.2% and 74.4% after one or two applications at 250 g a.i./ha at a 13-day interval (Day 0, fresh residues)	399 g a.i./ha (sweet corn use)	>1.6	Exceeded
			303 g a.i./ha (dry legume use)	>1.2	Exceeded
Green lacewing (*Chrysoperla carnea*)	Semi-field	No significant effects on mortality and fecundity after one or two applications at 250 g a.i./ha at a 13-day interval.			
Vascular plants					
Corn (*Zea mays*), oat (*Avena sativa*), onion (*Allium cepa*), ryegrass (*Lolium perenne*), cucumber (*Cucumis sativa*), oilseed rape (*Brassica napus*), pea (*Pisum sativum*), soybean (*Glycine max*), sugar beet (*Beta vulgaris*), and tomato (*Lycopersicon esculentum*)	Seedling emergence	EC_{25} >500 g a.i./ha	On-field: 614 g a.i./ha (sweet corn use)	<1.2	Possibly slightly exceeded
			Off-field (aerial application; 23% of sweet corn rate): 141 g a.i./ha	<0.3	Not exceeded
			Off-field (ground application; 6% of sweet corn rate): 37 g a.i./ha	<0.07	Not exceeded
			384 g a.i./ha (dry legume use)	<0.8	Not exceeded
	Vegetative vigour	EC_{25} >500 g a.i./ha	399 g a.i./ha (sweet corn use)	<0.8	Not exceeded
			303 g a.i./ha (dry legume use)	<0.6	Not exceeded

[1] EEC from the use on sweet corn, unless otherwise noted.
[2] Endpoint derived according to Atkins (1981), whereby LD_{50} µg/bee x 1.12 = LD_{50} kg/ha.
[3] For studies with *T. pyri* or *A. rhopalosiphi* where test material is sprayed on glass plates, the level of concern is exceeded when the risk quotient is ≥2.

Table 13 Screening level risk assessment of picoxystrobin for birds and mammals for the use with the maximum seasonal rate of application (sweet corn)

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)[a]	RQ	Level of Concern
Sweet corn (maximum cumulative seasonal rate of 399 g a.i./ha)					
Small Bird (0.02 kg)					
Acute	48.6	Insectivore (small insects)	20.08	0.41	Not exceeded
Reproduction	110.3	Insectivore (small insects)	20.08	0.18	Not exceeded
Medium Sized Bird (0.1 kg)					
Acute	48.6	Insectivore (small insects)	15.67	0.32	Not exceeded

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw) [a]	RQ	Level of Concern
Reproduction	110.3	Insectivore (small insects)	15.67	0.14	Not exceeded
Large Sized Bird (1 kg)					
Acute	48.6	Herbivore (short grass)	16.35	0.34	Not exceeded
Reproduction	110.3	Herbivore (short grass)	16.35	0.15	Not exceeded
Small Mammal (0.015 kg)					
Acute	500	Insectivore (small insects)	11.55	<0.02	Not exceeded
Reproduction	80	Insectivore (small insects)	11.55	0.14	Not exceeded
Medium Sized Mammal (0.035 kg)					
Acute	500	Herbivore (short grass)	36.19	<0.07	Not exceeded
Reproduction	80	Herbivore (short grass)	36.19	0.45	Not exceeded
Large Sized Mammal (1 kg)					
Acute	500	Herbivore (short grass)	19.34	<0.04	Not exceeded
Reproduction	80	Herbivore (short grass)	19.34	0.24	Not exceeded

[a] EDE = Estimated dietary exposure; is calculated using the following formula: (FIR/bw) x EEC, where:
FIR: Food Ingestion Rate (Nagy, 1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used:
Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = 0.398(bw in g) $^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(bw in g) $^{0.651}$.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235(bw in g) $^{0.822}$
bw: Generic Body Weight
EEC: Concentration of pesticide on food item based on Hoerger and Kenaga (1972) and Kenaga (1973) and modified according to Fletcher et al. (1994). At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used.

Table 14 Toxicity of picoxystrobin, a 250 g a.i./L Soluble Concentrate formulation and major transformation products to aquatic species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
Freshwater species					
Daphnia magna	48h-Acute	Picoxystrobin	EC_{50}: 24 µg a.i./L NOEC: 18 µg a.i./L	Very highly toxic	1893450
	48-h Acute	Picoxystrobin	LC_{50}: 18 µg a.i./L NOEC: not reported	Very highly toxic	1966840
	48h-Acute	250 g a.i./L SC formulation	EC_{50}: 86 µg/L (20 µg a.i./L); NOEC: 56 µg/L (13 µg a.i./L)	Very highly toxic	1893449
	48-h Acute	R403092 / Compound 2	EC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966830
	48-h Acute	R403814 / Compound 3	EC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966833
	48-h Acute	R408509 / Compound 8	EC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966836
	48-h Acute	R408631 / Compound 7	EC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966828
	48-h Acute	R413834 / Compound 26	EC_{50}: 8 mg/L NOEC: 3.8 mg/L	Moderately toxic	1966839

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
	21d-Chronic	Picoxystrobin	LC_{50}: 26 µg a.i./L NOEC (live young per parent): 8 µg a.i./L	No classification	1893457
Daphnia pulex	48-h Acute	Picoxystrobin	LC_{50}: >50 µg a.i./L	At worst, very highly toxic	1966840
Planarian (*Dugesia* sp.)	48-h Acute	Picoxystrobin	LC_{50}: 200-1000 µg a.i./L	Highly toxic	1966840
Planarian (*Polycelis* sp.)	48-h Acute	Picoxystrobin	LC_{50}: 200-1000 µg a.i./L	Highly toxic	1966840
Freshwater rotifer (*Brachionus calcyciflorus*)	24-h Acute	Picoxystrobin	LC_{50}: >4000 µg a.i./L	At worst, moderately toxic	1966840
Freshwater snail (*Limnea stagnalis*)	48-h Acute	Picoxystrobin	LC_{50}: >1000 µg a.i./L	At worst, moderately toxic	1966840
Tubificidae (a mixture of *Limnodrilus hofmeisteri* and *Tubifex* sp.)	48-h Acute	Picoxystrobin	LC_{50}: 299 µg a.i./L	Highly toxic	1966840
Leech (*Erpobdella octoculata*)	48-h Acute	Picoxystrobin	LC_{50}: 200-1000 µg a.i./L	Highly toxic	1966840
Mayfly nymph (*Cloeon dipterum*)	48-h Acute	Picoxystrobin	LC_{50}: 194 µg a.i./L	Highly toxic	1966840
Damselfly nymph (*Coenagrion puella*)	48-h Acute	Picoxystrobin	LC_{50}: >1000 µg a.i./L	At worst, moderately toxic	1966840
Cased caddisfly larvae (*Agrypnia varia*)	48-h Acute	Picoxystrobin	LC_{50}: 158 µg a.i./L	Highly toxic	1966840
phantom midge larva (*Chaoborus crystallinus*)	48-h Acute	Picoxystrobin	LC_{50}: 332 µg a.i./L	Highly toxic	1966840
Midge, 2nd instar larva (*Chironomus riparius*)	48-h Acute	Picoxystrobin	LC_{50}: 326 µg a.i./L	Highly toxic	1966840
Water-boatman, adult (*Notonecta* sp.)	48-h Acute	Picoxystrobin	LC_{50}: >1000 µg a.i./L	At worst, moderately toxic	1966840
Creeping water bug, adult (Naucoridae)	48-h Acute	Picoxystrobin	LC_{50}: >1000 µg a.i./L	At worst, moderately toxic	1966840
Cyclopoid copepods, adults (*Macrocyclops fuscus*)	48-h Acute	Picoxystrobin	LC_{50}: 87 µg a.i./L	Very highly toxic	1966840
Calanoid copepods, adults (*Diaptomus* sp.)	48-h Acute	Picoxystrobin	LC_{50}: 5 µg a.i./L	Very highly toxic	1966840
Water louse, juvenile (*Asellus aquaticus*)	48-h Acute	Picoxystrobin	LC_{50}: 152 µg a.i./L	Highly toxic	1966840
Freshwater	48-h Acute	Picoxystrobin	LC_{50}: 63 µg a.i./L	Very highly	1966840

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
shrimp, juvenile (*Crangonyx pseudogracilis*)				toxic	
Midge (*Chironomus riparius*)	28-d Chronic, spiked sediment	Picoxystrobin	Total emergence: EC_{50}: 19 mg a.i./kg dry weight; NOEC: 5.0 mg a.i./kg dry weight Based on mean-measured water concentrations: EC_{50}: 240 µg a.i./L NOEC: 40 µg a.i./L	No classification	1893542
	25-d Chronic, spiked water	Picoxystrobin	Total emergence: Mean measured concentration: EC_{50}: 56.4 µg a.i./L NOEC: 19.6 µg a.i./L Day 0 measured concentration (as per OECD 219): EC_{50}: 135 µg a.i./L NOEC: 54 µg a.i./L	No classification	1893453
Rainbow trout (*Oncorhynchus mykiss*)	96h-Acute	Picoxystrobin	LC_{50}: 70 µg a.i./L NOEC (mortality): 49 µg a.i./L; NOEC (discolouration): 14 µg a.i./L	Very highly toxic	1893456
	96-h Acute	250 g a.i./L SC formulation	LC_{50}: 0.22 mg/L (equivalent to 51 µg a.i./L); NOEC (mortality and sublethal effects): 0.15 mg/L (equivalent to 35 µg a.i./L)	Highly toxic	1893455
	96-h Acute	R413834/ Compound 26	LC_{50}: >10 mg/L NOEC: 10 mg/L	Practically non-toxic	1966838
	28-d Chronic	Picoxystrobin	LC_{50}: 27 µg a.i./L NOEC (mortality and sublethal effects): 10 µg a.i./L	No classification	1966820
Bluegill sunfish (*Lepomis macrochirus*)	96-h Acute	Picoxystrobin	LC_{50}: 77 µg a.i./L NOEC: 46 µg a.i./L	Very highly toxic	1893454
Mirror carp (*Cyprinus carpio*)	96-h Acute	Picoxystrobin	LC_{50}: 160 µg a.i./L NOEC: 110 µg a.i./L	Highly toxic	1966816
Three-spined stickleback (*Gasterosteus aculeatus*)	96-h Acute	Picoxystrobin	LC_{50}: 100 µg a.i./L (nominal) NOEC: 56 µg a.i./L	Highly toxic	1966818
Fathead minnow	96-h Acute	Picoxystrobin	LC_{50}: 65 µg a.i./L	Very highly	1966817

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
(*Pimephales promelas*)			NOEC: 56 µg a.i./L	toxic	
	96-h Acute, with sediment	Picoxystrobin	LC_{50}: 56.8 µg a.i./L (based on initial measured concentrations) NOEC: 49 µg a.i./L	Very highly toxic	1966822
	96-h Acute	R403092/ Compound 2	LC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966829
	96-h Acute	R403814/ Compound 3	LC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966831
	96-h Acute	R408509/ Compound 8	LC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966835
	96-h Acute	R408631/ Compound 7	LC_{50}: >10 mg/L NOEC: 10 mg/L	At worst, slightly toxic	1966827
	36-d Early Life Stage	Picoxystrobin	NOEC: 36 µg a.i./L (embryo hatching success, larval survival at 32 d post-hatch and larval growth (total length and wet weight) at test termination	No classification	1893459
Green algae (*Selenastrum capricornutum*)	72-h Acute	Picoxystrobin	EC_{50}: 32.8 µg a.i./L (yield, growth rate) NOEC: 4.4 µg a.i./L (cell density and yield)	No classification	1966815
	72-h Acute	250 g/L SC formulation	EC_{50}: 0.16 mg /L (40 µg a.i./L) (cell density and yield); NOEC: 0.045 mg/L (10 µg a.i./L) (all endpoints)	No classification	1966821
	72-h Acute	R403092/ Compound 2	EC_{50}: >10 mg/L (all endpoints); NOEC: 10 mg/L	No classification	1966824
	72-h Acute	R403814/ Compound 3	EC_{50}: >10 mg/L (all endpoints); NOEC: <10 mg/L	No classification	1966825
	72-h Acute	R408509/ Compound 8	EC_{50}: >10 mg/L (all endpoints); NOEC: <10 mg/L	No classification	1966826
	72-h Acute	R408631/ Compound 7	EC_{50}: >10 mg/L (all endpoints) NOEC: <10 mg/L	No classification	1966823
	72-h Acute	R413834/ Compound 26	EC_{50}: >10 mg/L (all endpoints) NOEC: <10 mg/L	No classification	1966837
Blue-green algae (*Anabaena flos-aquae*)	96-h Acute	Picoxystrobin	EC_{50}: >3000 µg a.i./L (all endpoints) NOEC: 3 µg a.i./L	No classification	1893564
Duckweed (*Lemna gibba*)	7-d Dissolved	Picoxystrobin	EC_{50}: 230 µg a.i./L (yield from frond density) NOEC: 49 µg a.i./L	No classification	1893563

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[1]	Reference
			(all endpoints)		
Microcosm with phytoplankton, zooplankton and macroinvertebrates	126-d Chronic	250 g a.i./L SC formulation	NOAEEC: 12 µg a.i./L (effects on zooplankton and macroinvertebrates)	No classification	1893462
Marine/estuarine species					
Mysid shrimp (*Americamysis bahia*)	96-h Acute	Picoxystrobin	LC_{50}: 33 µg a.i./L NOEC: 24 µg a.i./L (mortality and sublethal effects)	Very highly toxic	1893452
	29-d Chronic	Picoxystrobin	NOEC: 3.6 µg a.i./L (young per adult)	No classification	1893458
Eastern oyster (*Crassostrea virginica*)	96-h Acute	Picoxystrobin	Shell deposition: EC_{50}: 5.7 µg a.i./L NOEC: <1.4 µg a.i./L	Very highly toxic	1893451
Sheepshead minnow (*Cyprinodon variegatus*)	96-h Acute	Picoxystrobin	LC_{50}: 330 µg a.i./L NOEC (mortality): 200 µg a.i./L	Highly toxic	1893453
	33-d Early Life Stage	Picoxystrobin	NOEC (length and weight): 21 µg a.i./L	No classification	1893460
Saltwater diatom (*Skeletonema costatum*)	96-h Acute	Picoxystrobin	EC_{50}: 4 µg a.i./L (yield) NOEC: 2.3 µg a.i./L (all endpoints)	No classification	1893562

[1] US EPA classification where applicable

Table 15 Screening level risk assessment of picoxystrobin to aquatic organisms

Organism	Exposure	Endpoint value	EEC	RQ	Level of Concern
Freshwater species					
Aquatic invertebrates	Acute	HC_5 = 16 µg a.i./L	Sweet corn use: 85 µg a.i./L	5.3	Exceeded
			Dry legume use: 51 µg a.i./L	3.2	Exceeded
Daphnia magna	Chronic	NOEC = 8 µg a.i./L	Sweet corn use: 85 µg a.i./L	10.6	Exceeded
			Dry legume use: 51 µg a.i./L	6.4	Exceeded
Midge (*Chironomus riparius*)	Chronic, spiked water	NOEC = 19.6 µg a.i./L	Sweet corn use: 85 µg a.i./L	4.3	Exceeded
			Dry legume use: 51 µg a.i./L	2.6	Exceeded
Freshwater fish	Acute	HC_5 = 44.7 µg a.i./L	Sweet corn use: 85 µg a.i./L	1.9	Exceeded
			Dry legume use: 51 µg a.i./L	1.1	Exceeded
Fathead minnow (*Pimephales promelas*)	Chronic	NOEC = 10 µg a.i./L	Sweet corn use: 85 µg a.i./L	8.5	Exceeded
			Dry legume use: 51 µg a.i./L	5.1	Exceeded

Organism	Exposure	Endpoint value	EEC	RQ	Level of Concern
	Early Life Stage	NOEC = 36 µg a.i./L	Sweet corn use: 85 µg a.i./L	2.4	Exceeded
			Dry legume use: 51 µg a.i./L	1.4	Exceeded
Amphibians	Acute	HC_5 = 44.7 µg a.i./L	Sweet corn use: 454 µg a.i./L	10.2	Exceeded
			Dry legume use: 271 µg a.i./L	6.1	Exceeded
	Chronic	NOEC = 10 µg a.i./L	Sweet corn use: 454 µg a.i./L	45.4	Exceeded
			Dry legume use: 271 µg a.i./L	27.1	Exceeded
	Early Life Stage	NOEC = 36 µg a.i./L	Sweet corn use: 454 µg a.i./L	12.6	Exceeded
			Dry legume use: 271 µg a.i./L	7.5	Exceeded
Green algae (*Selenastrum capricornutum*)	Acute	$EC_{50}/2$ = 16.4 µg a.i./L	Sweet corn use: 85 µg a.i./L	5.2	Exceeded
			Dry legume use: 51 µg a.i./L	3.1	Exceeded
Duckweed (*Lemna gibba*)	Dissolved	$EC_{50}/2$ = 115 µg a.i./L	Sweet corn use: 85 µg a.i./L	0.7	Not exceeded
			Dry legume use: 51 µg a.i./L	0.4	Not exceeded
Marine species					
Mysid shrimp (*Americamysis bahia*)	Acute	$LC_{50}/2$ = 16.5 µg a.i./L	Sweet corn use: 85 µg a.i./L	5.2	Exceeded
			Dry legume use: 51 µg a.i./L	3.1	Exceeded
	Chronic	NOEC = 3.6 µg a.i./L	Sweet corn use: 85 µg a.i./L	23.6	Exceeded
			Dry legume use: 51 µg a.i./L	14.2	Exceeded
Eastern oyster (*Crassostrea virginica*)	Acute	$EC_{50}/2$ = 2.9 µg a.i./L	Sweet corn use: 85 µg a.i./L	29.3	Exceeded
			Dry legume use: 51 µg a.i./L	17.6	Exceeded
Sheepshead minnow (*Cyprinodon variegatus*)	Acute	$LC_{50}/10$ = 33 µg a.i./L	Sweet corn use: 85 µg a.i./L	2.6	Exceeded
			Dry legume use: 51 µg a.i./L	1.5	Exceeded
	Early Life Stage	NOEC = 21 µg a.i./L	Sweet corn use: 85 µg a.i./L	4.0	Exceeded
			Dry legume use: 51 µg a.i./L	2.4	Exceeded
Saltwater diatom (*Skeletonema costatum*)	Acute	$EC_{50}/2$ = 2 µg a.i./L	Sweet corn use: 85 µg a.i./L	42.5	Exceeded
			Dry legume use: 51 µg a.i./L	25.5	Exceeded

Table 16 Risk quotients for aquatic organisms determined for drift of picoxystrobin from aerial or field sprayer application on sweet corn and dry legumes using ASAE medium droplet size

Organism (exposure)	Endpoint (µg a.i./L)	Use pattern	Refined EEC (µg a.i./L)	RQ	Level of Concern
Aquatic invertebrates (Acute; 24-48 hrs)	HC_5 = 16 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	1.2	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.3	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.7	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.2	Not exceeded
Daphnia magna (Chronic; 21-d)	NOEC = 8 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	2.4	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.6	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	1.5	Exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.4	Not exceeded
Midge (*Chironomus riparius*) (Chronic, 25-d)	NOEC = 19.6 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	1.0	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.3	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.6	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.2	Not exceeded
Freshwater fish (Acute; 96-h)	HC_5 = 44.7 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	0.4	Not exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.1	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.3	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.1	Not exceeded
Fathead minnow (*Pimephales promelas*) (Chronic; 28-d)	NOEC = 10 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	2.0	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.5	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	1.2	Exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.3	Not exceeded
Fathead minnow (*Pimephales promelas*) (Early Life Stage; 36-d)	NOEC = 36 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	0.5	Not exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.1	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.3	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.1	Not exceeded
Amphibians (Acute, 96-h fish data)	HC_5 = 44.7 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 104 µg a.i./L	2.3	Exceeded
			Ground appl. (6% drift): 27.2 µg a.i./L	0.6	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 62.3 µg a.i./L	1.4	Exceeded
			Ground appl. (6% drift): 16.3 µg a.i./L	0.4	Not exceeded

Organism (exposure)	Endpoint (µg a.i./L)	Use pattern	Refined EEC (µg a.i./L)	RQ	Level of Concern
Amphibians (Chronic, 28-d, fish data)	NOEC = 10 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 104 µg a.i./L	10.4	Exceeded
			Ground appl. (6% drift): 27.2 µg a.i./L	2.7	Exceeded
		Dry legumes	Aerial appl. (23% drift): 62.3 µg a.i./L	6.2	Exceeded
			Ground appl. (6% drift): 16.3 µg a.i./L	1.6	Exceeded
Amphibians (Early Life Stage, 36-d, fish data)	NOEC = 36 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 104 µg a.i./L	2.9	Exceeded
			Ground appl. (6% drift): 27.2 µg a.i./L	0.8	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 62.3 µg a.i./L	1.7	Exceeded
			Ground appl. (6% drift): 16.3 µg a.i./L	0.5	Not exceeded
Green algae (*Selenastrum capricornutum*) (Acute, 72-h)	$EC_{50}/2$ = 16.4 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	1.2	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.3	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.7	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.2	Not exceeded
Marine species					
Mysid shrimp (*Americamysis bahia*) (Acute, 96-h)	$LC_{50}/2$ = 16.5 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	1.2	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.3	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.7	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.2	Not exceeded
Mysid shrimp (*Americamysis bahia*) (Chronic, 29-d)	NOEC = 3.6 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	5.4	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	1.4	Exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	3.3	Exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.9	Not exceeded
Eastern oyster (*Crassostrea virginica*) (Acute, 96-h)	$EC_{50}/2$ = 2.9 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	6.8	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	1.8	Exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	4.0	Exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	1.1	Exceeded
Sheepshead minnow (*Cyprinodon variegatus*) (Acute, 96-h)	$LC_{50}/10$ = 33 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	0.6	Not exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.2	Not exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.4	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.1	Not exceeded
Sheepshead minnow	NOEC = 21 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	0.9	Not exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	0.2	Not exceeded

Organism (exposure)	Endpoint (µg a.i./L)	Use pattern	Refined EEC (µg a.i./L)	RQ	Level of Concern
(*Cyprinodon variegatus*) (Early Life Stage, 33-d)		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	0.6	Not exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	0.1	Not exceeded
Saltwater diatom (*Skeletonema costatum*) (Acute, 96-h)	$EC_{50}/2$ = 2 µg a.i./L	Sweet corn	Aerial appl. (23% drift): 19.6 µg a.i./L	9.8	Exceeded
			Ground appl. (6% drift): 5.1 µg a.i./L	2.6	Exceeded
		Dry legumes	Aerial appl. (23% drift): 11.7 µg a.i./L	5.9	Exceeded
			Ground appl. (6% drift): 3.1 µg a.i./L	1.5	Exceeded

Table 17 Risk quotient for aquatic organisms as determined for run-off of picoxystrobin in water bodies 80 cm or 15 cm deep

Organism (exposure)	Endpoint value	EEC 90th percentile concentrations (time-frame)	RQ	Level of Concern
Freshwater species				
Aquatic invertebrates (Acute, 24-48 h)	HC_5 = 16 µg a.i./L	Sweet corn use (Peak): 7.1 µg a.i./L	0.4	Not exceeded
		Dry legume use (Peak): 4.6 µg a.i./L	0.3	Not exceeded
Daphnia magna (Chronic, 21-d)	NOEC = 8 µg a.i./L	Sweet corn use (21-d): 4 µg a.i./L	0.5	Not exceeded
		Dry legume use (21-d): 2.9 µg a.i./L	0.4	Not exceeded
Midge (*Chironomus riparius*) (Chronic, 25-d)	NOEC = 19.6 µg a.i./L	Sweet corn use (21-d): Overlying water: 4 µg a.i./L Pore water: 2.3 µg a.i./L	0.2 0.1	Not exceeded
		Dry legume use (21-d): Overlying water: 2.9 µg a.i./L Pore water: 1.4 µg a.i./L	0.2 0.09	Not exceeded
Freshwater fish (Acute, 96-h)	HC_5 = 44.7 µg a.i./L	Sweet corn use (96-h): 6.1 µg a.i./L	0.1	Not exceeded
		Dry legume use (96-h): 3.9 µg a.i./L	0.09	Not exceeded
Fathead minnow (*Pimephales promelas*) (Chronic, 28-d)	NOEC = 10 µg a.i./L	Sweet corn use (21-d): 4 µg a.i./L	0.4	Not exceeded
		Dry legume use (21-d): 2.9 µg a.i./L	0.3	Not exceeded
Fathead minnow (*Pimephales promelas*) (Early Life Stage, 36-d)	NOEC = 36 µg a.i./L	Sweet corn use (21-d): 4 µg a.i./L	0.1	Not exceeded
		Dry legume use (21-d): 2.9 µg a.i./L	0.08	Not exceeded
Amphibians Acute, 96-h, fish data)	HC_5 = 44.7 µg a.i./L	Sweet corn use (96-h, 15 cm): 15 µg a.i./L	0.3	Not exceeded
		Dry legume use (96-h, 15 cm): 9.5 µg a.i./L	0.2	Not exceeded
Amphibians (Chronic, 28-d, fish	NOEC = 10 µg a.i./L	Sweet corn use (21-d, 15 cm): 5.7 µg a.i./L	0.6	Not exceeded

Organism (exposure)	Endpoint value	EEC 90th percentile concentrations (time-frame)	RQ	Level of Concern
data)		Dry legume use (21-d, 15 cm): 4.2 µg a.i./L	0.4	Not exceeded
Amphibians (Early Life Stage, 36-d, fish data)	NOEC = 36 µg a.i./L	Sweet corn use (21-d, 15 cm): 5.7 µg a.i./L	0.2	Not exceeded
		Dry legume use (21-d, 15 cm): 4.2 µg a.i./L	0.1	Not exceeded
Green algae (*Selenastrum capricornutum*) (Acute, 72-h)	EC_{50}/2 = 16.4 µg a.i./L	Sweet corn use (Peak): 7.1 µg a.i./L	0.4	Not exceeded
		Dry legume use (Peak): 4.6 µg a.i./L	0.3	Not exceeded
Marine species				
Mysid shrimp (*Americamysis bahia*) (Acute, 96-h)	LC_{50}/2 = 16.5 µg a.i./L	Sweet corn use (96-h): 0.78 µg a.i./L	0.05	Not exceeded
		Dry legume use (96-h): not determined[1]		
Mysid shrimp (*Americamysis bahia*) (Chronic, 29-d)	NOEC = 3.6 µg a.i./L	Sweet corn use (21-d): 0.47 µg a.i./L	0.1	Not exceeded
		Dry legume use (21-d): not determined[1]		
Eastern oyster (*Crassostrea virginica*) (Acute, 96-h)	EC_{50}/2 = 2.9 µg a.i./L	Sweet corn use (96-h): 0.78 µg a.i./L	0.3	Not exceeded
		Dry legume use (96-h): not determined[1]		
Sheepshead minnow (*Cyprinodon variegatus*) (Acute, 96-h)	LC_{50}/10 = 33 µg a.i./L	Sweet corn use (96-h): 0.78 µg a.i./L	0.02	Not exceeded
		Dry legume use (96-h): not determined[1]		
Sheepshead minnow (*Cyprinodon variegatus*) (Early Life Stage, 33-d)	NOEC = 21 µg a.i./L	Sweet corn use (21-d): 0.47 µg a.i./L	0.02	Not exceeded
		Dry legume use (21-d): not determined[1]		
Saltwater diatom (*Skeletonema costatum*) (Acute, 96-h)	EC_{50}/2 = 2 µg a.i./L	Sweet corn use (96-h): 0.78 µg a.i./L	0.4	Not exceeded
		Dry legume use (96-h): not determined[1]		

[1] EECs as a result of picoxystrobin use on dry legumes were not generated, as the hectarage of these crops grown in coastal areas like British Columbia and Atlantic Canada was small. Exposure estimates from sweet corn use will cover off those for dry legumes, as the cumulative seasonal rates of application to sweet corn are higher than those for dry legumes.

Table 18 Screening level risk assessment of transformation products of picoxystrobin to freshwater aquatic organisms from the proposed use on sweet corn

Organism	Exposure	Endpoint value	EEC	RQ	Level of Concern
Compound 2					
Daphnia magna	Acute	EC_{50}/2 >5000 µg/L	82 µg/L	<0.02	Not exceeded
Fathead minnow (*Pimephales promelas*)	Acute	LC_{50}/10 >1000 µg/L	82 µg/L	<0.08	Not exceeded
Amphibian (fish data used as a surrogate)	Acute	LC_{50}/10 > 1000 µg/L	437 µg/L	<0.4	Not exceeded
Green algae	Acute	EC_{50}/2 > 5000 µg/L	82 µg/L	<0.02	Not exceeded

Organism	Exposure	Endpoint value	EEC	RQ	Level of Concern
(*Selenastrum capricornutum*)					
Compound 3					
Daphnia magna	Acute	EC_{50}/2 >5000 µg/L	38 µg/L	<0.008	Not exceeded
Fathead minnow (*Pimephales promelas*)	Acute	LC_{50}/10 > 1000 µg/L	38 µg/L	<0.04	Not exceeded
Amphibian (fish data used as a surrogate)	Acute	LC_{50}/10 > 1000 µg/L	202 µg/L	<0.2	Not exceeded
Green algae (*Selenastrum capricornutum*)	Acute	EC_{50}/2 >5000 µg/L	38 µg/L	<0.008	Not exceeded
Compound 8					
Daphnia magna	Acute	EC_{50}/2 >5000 µg/L	69 µg/L	<0.01	Not exceeded
Fathead minnow (*Pimephales promelas*)	Acute	LC_{50}/10 >1000 µg/L	69 µg/L	<0.07	Not exceeded
Amphibian (fish data used as a surrogate)	Acute	LC_{50}/10 >1000 µg/L	367	<0.4	Not exceeded
Green algae (*Selenastrum capricornutum*)	Acute	EC_{50}/2 >5000 µg/L	69 µg/L	<0.01	Not exceeded
Compound 7					
Daphnia magna	Acute	EC_{50}/2 >5000 µg/L	72 µg/L	<0.01	Not exceeded
Fathead minnow (*Pimephales promelas*)	Acute	LC_{50}/10 >1000 µg/L	72 µg/L	<0.07	Not exceeded
Amphibian (fish data used as a surrogate)	Acute	LC_{50}/10 >1000 µg/L	385 µg/L	<0.4	Not exceeded
Green algae (*Selenastrum capricornutum*)	Acute	EC_{50}/2 >5000 µg/L	72 µg/L	<0.01	Not exceeded
Compound 26					
Daphnia magna	Acute	EC_{50}/2 = 4000 µg/L	41 µg/L	0.01	Not exceeded
Rainbow trout (*Oncorhynchus mykiss*)	Acute	LC_{50}/10 >1000 µg/L	41 µg/L	<0.04	Not exceeded
Amphibian (fish data used as a surrogate)	Acute	LC_{50}/10 >1000 µg/L	219 µg/L	<0.2	Not exceeded
Green algae (*Selenastrum capricornutum*)	Acute	EC_{50}/2 >5000 µg/L	41 µg/L	<0.008	Not exceeded

Table 19 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
Predominantly anthropogenic[2]	Yes		Yes
Persistence[3]:	Soil	Half-life ≥ 182 days	DT_{50} of 23.6 to 36.1 days

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints
	Water	Half-life ≥ 182 days	DT_{50} of 3.6 to 17.3 days in the water phase of aerobic and anaerobic water-sediment systems
	Sediment	Half-life ≥ 365 days	DT_{50} of 36.6 to 67.2 days in the sediment phase of aerobic and anaerobic water-sediment systems
	Air	Half-life ≥ 2 days or evidence of long range transport	Volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (0.0000055 Pa at 20°C) and Henry's Law Constant (6.13 x 10^{-9} atm·m^3/mol at 20°C).
Bioaccumulation[4]	Log K_{OW} ≥ 5		Log K_{OW} = 3.6
	BCF ≥ 5000		BCF = 290
	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 20 Registered alternative products for the crops and pests proposed for registration on the DuPont Acapela Fungicide label. Please note that some active ingredients may not be registered on the entire crop group.

Crop/Crop Group	Pest(s)	Alternative Chemical Classes (Mode of Action Group)
Cereals (wheat, barley, oats, rye, triticale)	leaf rust	propiconazole (3) prothioconazole (3) tebuconazole (3) metconazole (3) azoxystrobin (11) pyraclostrobin (11) trifloxystrobin (11) mancozeb (M)
	septoria leaf blotch	propiconazole (3) prothioconazole (3) tebuconazole (3) metconazole (3) azoxystrobin (11) pyraclostrobin (11) trifloxystrobin (11) chlorothalonil (M) mancozeb (M)
	powdery mildew	propiconazole (3) triadimenol (3) pyraclostrobin (11) trifloxystrobin (11)
	tan spot (wheat)	propiconazole (3)

Crop/Crop Group	Pest(s)	Alternative Chemical Classes (Mode of Action Group)
		prothioconazole (3) tebuconazole (3) metconazole (3) azoxystrobin (11) pyraclostrobin (11) trifloxystrobin (11) chlorothalonil (M) mancozeb (M)
Corn (field, sweet, seed, popcorn)	northern corn leaf blight	propiconazole (3) azoxystrobin (11)
Soybean	Asian soybean rust	propiconazole (3) metconazole (3) azoxystrobin (11) pyraclostrobin (11) *Bacillus subtilis* (44)
	frogeye leafspot	propiconazole (3) pyraclostrobin (11) *Bacillus subtilis* (44)
	brown spot	*Bacillus subtilis* (44)
	sclerotinia stem rot	fluazinam (29) *Coniothyrium minitans* (NC)
Dry legumes	Asian soybean rust	azoxystrobin (11) pyraclostrobin (11)
	mycosphaerella blight (pea)	azoxystrobin (11) pyraclostrobin (11) boscalid (7)
	white mould	thiophanate-methyl (1) iprodione (2) vinclozin (2) boscalid (7) cyprodinil (9) + fludioxonil (12) dicloran (14) fluazinam (29) *Bacillus subtilis* (44) *Coniothyrium minitans* (NC)

Table 21 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed use claim	Supported / Unsupported
Control of tan spot (*Pyrenophora trichostoma*) on cereals at a rate of 0.44 – 0.6 L/ha; under high disease pressure use 0.88 L/ha.	Supported at 0.44 – 0.88 L/ha on wheat only.
Control of powdery mildew (*Erysiphe graminis*) on cereals at a rate of 0.44 – 0.6 L/ha; under high disease pressure use 0.88 L/ha.	Supported at 0.44 – 0.88 L/ha on crop group.
Control of leaf rust (*Puccinia recondita*) on cereals at a rate of 0.44 – 0.6 L/ha; under high disease pressure use 0.88 L/ha.	Supported at 0.44 – 0.88 L/ha on wheat, rye and triticale.
Control of septoria leaf blotch (*Septoria* spp.) on cereals at a rate of 0.44 – 0.6 L/ha; under high disease pressure	Supported at 0.44 – 0.88 L/ha on wheat, barley, rye and triticale.

Proposed use claim	Supported / Unsupported
use 0.88 L/ha.	
Control of northern leaf blight (*Setosphaeria turcica*, *Exserohilum turcicum*) on corn at 0.44 – 0.8 L/ha.	Supported as proposed.
Control of asian soybean rust (*Phakopsora pachyrhizi*) on dry legumes at 0.6 – 0.88 L/ha.	Supported at proposed rates on crop group.
Control of white mould (*Sclerotinia sclerotiorum*) on dry legumes at 0.88 L/ha.	Supported as suppression at proposed rate on crop group. Two additional trials are required to confirm the level of efficacy.
Control of mycosphaerella blight (*Mycosphaerella pinodes*) on dry legumes at 0.6 – 0.88 L/ha.	Supported at proposed rates on field pea. One additional trial is required to confirm the level of efficacy.
Control of frogeye leafspot (*Cercospora sojina*) on soybeans at 0.44 – 0.88 L/ha.	Supported as proposed.
Control of asian soybean rust (*Phakopsora pachyrhizi*) on soybeans 0.44 – 0.88 L/ha.	Supported as proposed.
Control of sclerotinia stem rot (*Sclerotinia sclerotiorum*) on soybeans at 0.88 L/ha.	Supported as suppression at proposed rate. Two additional trials are required to confirm the level of efficacy.
Control of brown spot (*Septoria glycines*) on soybeans at 0.44 – 0.88 L/ha.	Supported at proposed rates. Two additional trials are required to confirm the level of efficacy.
Aerial application to all proposed crops at a minimum spray volume of 40 L water/ha.	Supported on proposed crops at a minimum spray volume of 50 L water /ha.

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

Picoxystrobin is a new active ingredient which is concurrently being registered in the US. The US EPA is in agreement with the specified Canadian MRLs and will be promulgating the same tolerances (*40 CFR Part 180*), except several commodities. Codex MRLs[10] (*Codex MRLs* searchable by pesticide or commodity) have not been established for picoxystrobin on any commodity.

Table 1 Differences Between Canadian MRLs and in Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex (ppm)
Barley bran	0.5	-	Not reviewed by Codex
Barley	0.3	0.3	
Wheat germ	0.09	0.09	
Crop Subgroup 20A (Rapeseed Subgroup)	0.08	0.08[a]	
Corn oil	0.07	0.07	
Crop Subgroup 6C (Dried Shelled Pea and Bean, except soybean)	0.06	0.06	
Wheat bran	0.06	0.06	
Dry soybeans	0.05	0.05	
Crop Group 15 (Cereal Grains, except barley and rice)	0.04	0.04	
Cream	-	0.01	
Eggs	0.01	-	
Fat, meat and meat by-products of cattle, goats, hogs, horses, poultry, and sheep	0.01	-	
Fat, meat and meat by-products (except kidney) of cattle, goats, horses, and sheep	-	0.01	
Milk	0.01	0.01	

[a] For canola only in the US.

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.

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

Under the North American Free Trade Agreement (NAFTA), 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.

References

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