Evaluation Report ERC2014-02

Fluopyram

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

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Overview

Registration Decision for Fluopyram

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of the technical active, Fluopyram Technical Fungicide and end-use products, Luna Privilege containing the technical grade active ingredient fluopyram, Luna Tranquility Fungicide containing the technical grade active ingredients fluopyram and pyrimethanil, and Propulse Fungicide containing the technical grade active ingredients fluopyram and prothioconazole. All three end-use products are used to control several fungal diseases on various horticultural and field crops.

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

Although the risks and value have been found acceptable when all risk reduction measures are followed, the applicant must submit additional scientific information as a condition of registration.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of fluopyram in Fluopyram Technical Fungicide, Luna Privilege, Luna Tranquility Fungicide and Propulse 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.

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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."

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 Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Is Fluopyram?

Fluopyram is a new systemic fungicidal compound present as the lone active ingredient in the new end-use product Luna Privilege. It is also present as one of the two active ingredients in two new pre-mix end-use products, Luna Tranquility Fungicide and Propulse Fungicide. The compound is used as a broad-spectrum fungicide applied as a foliar spray or through drip irrigation systems on various horticultural and field crops. It acts on pathogen cells by inhibiting their normal respiration process.

Health Considerations

Can Approved Uses of Fluopyram Affect Human Health?

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

Exposure to fluopyram may occur through the diet (food and water), 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 acute toxicity of fluopyram was low via the oral, dermal and inhalation routes of exposure. Fluopyram was minimally irritating to the eyes and non-irritating to the skin and did not cause an allergic skin reaction.

The acute toxicity of the end-use product Luna Privilege was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eyes and non-irritating to the skin and did not cause an allergic skin reaction. Both end-use products Luna Tranquility Fungicide and Propulse Fungicide were of low acute toxicity via the oral, dermal and inhalation routes of exposure. They were non-irritating to the eyes and skin and did not cause allergic skin reactions.

Health effects in animals given repeated doses of fluopyram included changes in the liver, thyroid and kidneys. Fluopyram did not cause birth defects in animals and there were no effects on the ability to reproduce. When fluopyram was given to pregnant or nursing animals, effects on the developing fetus and juvenile animal (reduced pup and litter weights, body size, spleen and thymus weights, and/or slightly delayed sexual development) were observed at doses that were toxic to the mother, indicating that the young do not appear to be more sensitive to fluopyram than the adult animal. Fluopyram did not selectively target the nervous system, however, temporary non-specific functional effects (decreased motor and locomotor activity) were observed, possibly related to the nervous system. There was no evidence to suggest that fluopyram damaged genetic material. Fluopyram did, however, cause thyroid tumours in mice and liver tumours in rats.

The risk assessment protects against the effects of fluopyram 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 infants less than one year old, the subpopulation which would ingest the most fluopyram relative to body weight, are expected to be exposed to less than 64% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from fluopyram is not of concern for all population subgroups. The lifetime cancer risk from the use of fluopyram on various crops is considered acceptable, based on a limited three-year application period.

Acute dietary (food and water) estimates for the general population and all population subgroups were less than 10% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was children 1-2 years old.

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

Residue trials conducted throughout Canada and the United States using fluopyram on potatoes, sugar beets, dry beans and dry peas, watermelon, apples, cherries, strawberries, grapes, almonds, pecans, peanuts, soybeans, wheat, sorghum, corn (field and sweet), canola and cottonseed, as well as trials conducted in Latin America using fluopyram on bananas are acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of this Evaluation Report.

Risks in Residential and Other Non-Occupational Environments

Residential risks are not of concern when products containing fluopyram are used according to the label directions.

Occupational Risks from Handling Luna Privilege, Propulse Fungicide and Luna Tranquility Fungicide

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

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

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

Environmental Considerations

What Happens When Fluopyram is Introduced into the Environment?

When fluopyram is applied as a fungicide on field crops, some of it finds its way into soil and water. In soils, it is persistent and has a potential for long-term accumulation and residue carry over to the following crop season. Fluopyram is stable to hydrolysis, photolysis, aerobic and anaerobic biotransformation in soils and does not form major transformation products in soils under Canadian field use conditions. Fluopyram is moderately mobile in soils and has a potential to leach and contaminate the groundwater depending on the soil type and location. None of the minor transformation products, however, have a potential to leach and contaminate groundwater. Fluopyram has a low potential for bioconcentration/bioaccumulation in organisms.

In the aquatic environment, fluopyram is persistent under aerobic and anaerobic conditions and partitions significantly from water to sediment. It does not form any major transformation products in water or sediment phases. Photolysis is not an important route of transformation in the aquatic environment. Several minor transformation products were detected due to photolysis under laboratory conditions in natural water of which one was identified as fluopyram-lactam.

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

Fluopyram presents a negligible risk to soil organisms, bees, beneficial arthropods, freshwater and marine fish, invertebrates, algae and aquatic plants. Fluopyram, however, may pose a risk to non-target terrestrial plants from spray drift (Luna Privilege only), and to amphibians due to runoff and spray drift. In order to minimize the potential risk, no-spray buffer zones between the treated area and downwind sensitive terrestrial and aquatic habitats are required. A bird toxicity label statement is also required as a precaution.

Value Considerations

What Is the Value of Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide?

Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide are fungicides effective in the control of major economic diseases of various horticultural and field crops.

Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide provide effective solutions for the management of major economic diseases such as powdery mildew, moulds, blights and other foliar diseases on a range of crops including potato, dry bean, chickpeas, lentils, apple, cherry, wine grape, strawberry, peanut, watermelon and almond. The combinations of different modes of action in Luna Tranquility Fungicide and Propulse Fungicide are of value in reducing the risk of resistance development and by increasing the spectrum of disease protection.

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 on the label of Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

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

Environment

Based on the risk identified to off-target sensitive habitats, buffer zones of 1 to 15 m are required to protect amphibians and terrestrial habitats. In addition, standard label statements were added to the labels to protect wild birds, aquatic organisms and non-target terrestrial plants.

What Additional Scientific Information Is Being Requested?

Although the risks and value have been found acceptable when all risk-reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information within the time frames indicated.

Human Health

- Short-term mode of action studies to address the observed tumours. The goal of these studies is to further clarify the two proposed cancer modes of action.
- Inter-Laboratory Analytical Methodology Validation – An independent laboratory validation of Method GM-001-P07-01 for the determination of fluopyram residues in plant matrices is required to fulfill the data requirement for an acceptable enforcement method in plant matrices.
- Field Accumulation Studies – A full set of field rotational crop data are required for canola, soybean and cereals (wheat, barley and corn, both field and sweet).

Value

- One field trial to confirm the efficacy of Luna Privilege against powdery mildew on standard sized cherry trees.
- One field trial to confirm efficacy of Luna Privilege against late leaf spot on peanuts.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted,[3] the PMRA will publish a consultation document when there is a proposed decision on applications to convert the conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (that is, the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

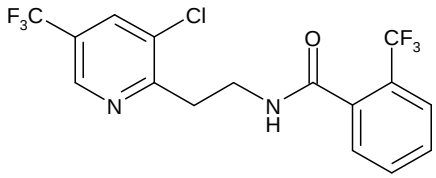
[3] As per subsection 28(1) of the *Pest Control Products Act.*

Science Evaluation

Fluopyram

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Fluopyram
Function	Fungicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	*N*-{2-[3-chloro-5-(trifluoromethyl)-2-pyridyl]ethyl}-α,α,α-trifluoro-*o*-toluamide
2. Chemical Abstracts Service (CAS)	Benzamide, N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)-
CAS number	658066-35-4
Molecular formula	$C_{16}H_{11}ClF_6N_2O$
Molecular weight	396.72 g/mol
Structural formula	
Purity of the active ingredient	98.6%

1.2 Physical and Chemical Properties of the Active Ingredients and End-use Product

Technical Product—Fluopyram Technical Fungicide

Property	Result
Colour and physical state	White powder
Odour	No noticeable odour
Melting range	118°C
Boiling point or range	319°C (correlated range) under decomposition
Relative Density	1.53
Vapour pressure at 20°C	1.2×10^{-6} Pa (20°C)
Henry's law constant at 20°C	2.98×10^{-5} Pa×m^3×mol^{-1}

Property	Result
Ultraviolet (UV)-visible spectrum	Acetonitrile: λ_{max} [nm] ε [L mol^{-1} cm^{-1}] 216 14877 270 4332.18 Acetonitrile pH = 2: λ_{max} [nm] ε [L mol^{-1} cm^{-1}] 208 16570.99 270 4399.62 Acetonitrile pH = 10: λ_{max} [nm] ε [L mol^{-1} cm^{-1}] 208 16892.34 270 4383.76 Water λ_{max} [nm] ε [L mol^{-1} cm^{-1}] 270 4577.053
Solubility in water at 20°C	16 mg/L (distilled water) 15 mg/L (pH 4) 16 mg/L (pH 7) 15 mg/L (pH 9)
Solubility in organic solvents at 20°C	Solvent Solubility (g/L) acetone >250 dichlorethane >250 dimethyl sulfoxide >250 ethyl acetate >250 n-heptane 0.66 methanol >250 toluene 62.2
n-Octanol-water partition coefficient (K_{ow})	log K_{ow} = 3.3 at 20°C
Dissociation constant (pK_a)	No dissociation observed between pH 2 and 12
Stability (temperature, metal)	Stable in presence of metals (iron and aluminum) and when stored for two weeks at 54°C in presence of metals and metal ions.

End-use Products–Fluopyram

Property	Result		
	Luna Privilege	**Luna Tranquility Fungicide**	**Propulse Fungicide**
Colour	Beige	Off-white	Off-white
Odour	Chemical odour	Wine-like odour	Mild sweet odour
Physical state	Liquid	Liquid	Liquid
Formulation type	Suspension	Suspension	Suspension
Guarantee	Fluopyram 500 g/L	Fluopyram 125 g/L Pyrimethanil 375 g/L	Fluopyram 200 g/L Prothioconazole 200 g/L
Container material and description	HDPE bottle/canister, 0.25 – 10 L, or canister/IBC such as 1000 L	HDPE containers, 1 to 200 L	HDPE containers, 1 to 200 L
Density	1.205 g/mL	1.11 g/mL	1.15 g/mL
pH of 1% dispersion in water	6.5	7.2	5.0
Oxidizing or reducing action	None	None	None
Storage stability	Stable over 12 months in HDPE packaging at ambient temperature.	Stable when stored for 12 months at ambient temperature in commercial packaging	Stable when stored for 12 months at ambient temperature in commercial packaging
Corrosion characteristics	Not corrosive	Not corrosive	Not corrosive
Explodability	Not explosive	Not explosive	Not explosive

1.3 Directions for Use

Luna Privilege, Luna Tranquility Fungicide and Propulse Fungicide are used for the control of powdery mildew, moulds, blights and other foliar diseases on various field and horticultural crops. The products are intended for foliar applications on all crops with the exception of strawberry where applications via chemigation are indicated for Luna Privilege. The application rate ranges for Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide, are 150-500 mL/ha, 600-1200 mL/ha and 500-750 mL/ha, respectively.

1.4 Mode of Action

Fluopyram is a new broad-spectrum systemic active ingredient classified as a group 7 fungicide (succinate dehydrogenase inhibitor) by the Fungicide Resistance Action Committee. Fluopyram interferes with the normal respiration process in the cells of pathogenic fungal cells. Fluopyram shows systemic and preventative activity against the ascomycetes, a group of fungi that includes many economically important crop pathogens.

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 Fluopyram Technical Fungicide have been validated and assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

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 (70-110%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

HPLC-MS/MS methods developed and proposed for data generation and enforcement purposes in plant and animal commodities fulfilled the requirements with regards to specificity, accuracy and precision at the respective limits of quantitation of the methods. Acceptable recoveries (70-120%) were obtained in plant and animal matrices. The proposed enforcement method for animal commodities was successfully validated in several animal matrices by an independent laboratory. Adequate extraction efficiencies were demonstrated using radiolabelled samples of several crop matrices and livestock tissues analyzed with the respective enforcement methods Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Fluopyram is a broad spectrum pyridylethylamide fungicide. A detailed review of the toxicological database for fluopyram was conducted. The database consists of the full array of toxicity studies currently required for hazard assessment purposes. The database also includes neurotoxicity and cancer mode of action (MOA) studies. In addition, an acute oral toxicity, a 28 day dietary toxicity and three genotoxicity studies were provided for a plant/soil metabolite. 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 fluopyram. However, additional information is being developed to further elucidate the cancer modes of action.

The absorption, distribution, metabolism and excretion characteristics of single and multiple radiolabelled doses, were evaluated in rats. Orally administered fluopyram was rapidly and extensively absorbed. Time to maximal tissue concentration varied from 0.8 to 15 hours depending on the placement of radiolabel and the dosing regime. The systemic exposure was proportional to the dose and slightly higher in females compared to males. Absorbed fluopyram was widely distributed, with the concentrations in the plasma being exceeded by the maximal levels in each of the following organs and tissues: the liver, kidneys, and Harderian gland in all test groups as well as the carcass, red blood cells, ovaries, thyroid and adrenals in some groups. Excretion of fluopyram was rapid and dose-independent. Fluopyram was eliminated predominantly via the bile, with appreciable amounts also excreted in the urine. After cessation of dosing, organ and tissue concentrations of radioactivity decreased rapidly. There was 0.3-6% of administered dose remaining in the carcass at 168 hours, depending on the radiolabel position, so the potential for accumulation cannot be ruled out. Fecal elimination was essentially complete within 96 hours. Elimination of fluopyram via respired volatiles and CO_2 was negligible. The initial elimination half-life ranged from 3.9 to 16.2 hours depending on the radiolabel position and dose level. The terminal elimination half-life increased to a range of 23.6 to 72.9 hours. There were no significant sex- or dose-related differences in the tissue distribution and retention or in the extent or route of elimination.

Fluopyram was extensively metabolized, with the ethyl linking group of the parent as the preferred site for metabolism, resulting in 7-hydroxy and 8-hydroxy metabolites. Further oxidation resulted in an -enol metabolite, which was further conjugated to glucuronic acid. Hydroxylation of the phenyl ring resulted in -phenol and 7-OH-phenol metabolites. Elimination of water from compounds hydroxylated in the ethylene bridge resulted in fluopyram-Z-olefine and E-olefine metabolites (E- and Z-olefine can isomerize into each other). As the double bond of olefine may be a target for epoxidation and a dihydroxy-metabolite (which could result from hydrolysis of an epoxide by epoxide hydrolase) was observed, the olefine was considered to be of potential toxicological significance. All of the hydroxylated metabolites were conjugated primarily to glucuronic acid and to a lesser extent with sulfate. The cleavage of the molecule yielded label-specific metabolites (-benzamide; -pyridyl-acetic acid, -ethyl-diol, -pyridyl carboxylic acid) that represented the most abundant metabolites. These metabolites were further metabolized via oxidation, hydroxylation and conjugation. The phenyl ring moiety was also conjugated with glutathione followed by further degradation to 7-OH-methyl-sulfone, -BA-methyl-sulfoxide and -BA-methyl-sulfone (phenyl label only).

There were sex differences in the quantity of metabolites generated. Fluopyram-7-hydroxy and 7-OH-phenol metabolites were higher in males than females. Females showed higher amounts of 8-hydroxy and -benzamide than males. Low dose females excreted more of phenyl specific -benzamide and -benzoic acid than males. Females treated with the pyridyl label excreted more -pyridyl-acetic acid than males, while males excreted more -ethyl-diol metabolites than females. Parent compound accounted for 0.4/1.9% ♂/♀ of the administered dose for the single oral low dose group and 10.5/16.7% ♂/♀ of the administered dose for the single oral high dose group. There were no significant differences in metabolism between the doses, or between single and repeat dosing.

The acute toxicity of the active ingredient fluopyram and its three end-use products was low via the oral, dermal and inhalation routes in rats. All four products were non-irritating to minimally irritating to the eyes and non-irritating to the skin of rabbits. None of the products were skin sensitizers in either guinea pigs or mice.

In the short-term oral studies, the liver was the main target organ in mice, rats and dogs. Hepatotoxicity manifested as increased liver weight, liver enlargement, darkening, necrosis and centrilobular and mid-zonal hepatocellular hypertrophy, as well as alterations in clinical chemistry (elevated plasma/serum levels of liver enzymes, cholesterol and/or phospholipids, and triglycerides with decreased albumin). The rat was the most sensitive species following short-term oral dosing. The liver toxicity between mice, rats and dogs was similar with the exceptions of dark livers in the rodents only, and increased cholesterol and hepatocellular macrovacuolation in rats only. Mice and dogs had hepatocellular necrosis, which was not observed in rats. In several studies, effects on the liver at lower doses were mild and considered to be non-adverse, reflecting an adaptive response of the liver rather than overt hepatotoxicity. The spectrum of liver effects and the doses eliciting hepatotoxicity worsened significantly with the duration of dosing (short-term to chronic). At higher doses in mice, decreased pigment and increased vacuolation of the adrenals were noted. For rats, higher dose levels resulted in decreased body weight, increased thyroid hormone levels, vacuolation in the adrenals, pale or dark kidneys, kidneys with cysts or cellular debris, follicular cell hypertrophy of the thyroid, increased thyroid weight, and decreased fore- and hindlimb grip strength. High doses in the dogs resulted in decreased body and thymus weight.

Dermal dosing of rats for 28 days resulted in increased prothrombin time, cholesterol, liver weight and minimal hepatocellular hypertrophy at 1000 mg/kg bw/day, the highest dose tested.

The liver, kidneys, and thyroid were the primary target organs in the mouse and rat with chronic oral dosing. With long-term dosing in mice, the thyroid exhibited increased incidences and severity of follicular cell hyperplasia. Liver enlargement and a variety of histopathological effects were also more frequently observed at doses lower than in the short-term study. At the highest dose tested, mouse body weights were decreased, kidney weights were slightly decreased and the incidence and severity of several renal histopathological effects were significantly increased. In rats, the same liver effects seen in the short-term studies were repeated at similar or lower dose levels. Additionally, altered hepatocyte foci and hepatocellular necrosis were identified following 12 and 24 months of treatment. In rat thyroids, the incidence and severity of follicular cell hypertrophy, hyperplasia and colloid alteration were increased. After 24 months the kidneys of male rats exhibited increased incidences and/or severities of chronic progressive nephropathy, tubular hyperplasia, hypertrophy or dilatation, and golden brown pigment. In rats, the eyes were also a target organ with corneal opacity and edema, opacity of the lens and small retinal vessels seen at relatively low dose levels. At the highest two doses tested in the 12- and 24-month rat studies, there were additional generalized findings such as decreased body weight, prostration, pallor, wasted appearance and hair loss.

Fluopyram was tested for in vitro and in vivo genotoxicity in a range of assays. Based on the negative results obtained in a battery of genotoxicity studies, fluopyram is considered unlikely to be genotoxic.

Tumours were observed in the mouse and the rat in the dietary oncogenicity studies. The dosing was considered adequate in these studies. Male mice had thyroid follicular cell adenomas while female rats had liver adenomas and carcinomas. These tumours are considered uncommon in the respective species/sex. The proposed MOA for the thyroid adenomas was chronic perturbation of

thyroid hormone homeostasis. In liver, the proposed MOA was phenobarbital-like liver proliferation. Cancer MOA studies were conducted to examine liver and thyroid effects in the rat and mouse. These studies in mice showed that fluopyram increased T4 elimination, but did not affect thyroid hormone synthesis. Fluopyram also up-regulated sulfotransferase and UDP glucuronosyltransferase transcripts in the liver. These transcripts are known to encode enzymes that inactivate T3 and T4. Additionally, P450, EROD, PROD, and BROD enzymes were increased in fluopyram treated mice. While the evidence was generally supportive for the thyroid tumour MOA, there are data gaps in terms of dose and time concordance between the MOA data and the tumourigenic dose levels. In female rats, hepatocellular hypertrophy and liver cell proliferation were associated with the induction of xenobiotic metabolizing enzymes. Again, while the evidence was generally supportive for the liver tumour MOA, there were data gaps. Overall, when the results from all of the MOA studies in mice and rats are considered, there was insufficient evidence to conclude that the oncogenic effects in the thyroid and liver were specific consequences of chronically perturbed thyroid hormone homeostasis and chronically induced liver metabolizing enzymes. A linear low dose extrapolation (Q_1*) approach was used for the cancer risk assessment in the absence of a sufficient weight of evidence to support a proposed threshold-based MOA.

No effects on reproduction were noted in a multigeneration reproduction study in the rat. There was a decrease in offspring body weight during early lactation in both generations at the highest dose tested. Also, at this dose, there were decreases in thymus and spleen weights, with no histopathological correlates. Effects were also observed in parental animals at the high dose and included decreased body weight and body weight gain, increased cholesterol and white blood cell counts, increased liver weight with centrilobular hepatocellular hypertrophy, increased kidney weight with nephropathy and lymphocytic infiltration, decreased spleen weight in the absence of histopathological changes, increased vacuolization in the adrenals and macrophages in the lungs. There was no evidence of sensitivity of the young.

In the oral developmental toxicity study in rats, the only fetal effects noted were decreased fetal weight, thymic remnants and four different skeletal variations at the highest dose tested. The dams exhibited decreased body weight gain and food consumption along with increased liver weights and centrilobular hepatocellular hypertrophy starting at the mid dose, plus decreased body weights and visibly enlarged livers at the high dose. In rabbits, fetal weights were decreased and the number of runts was increased at the highest dose tested. The does at that dose level had decreased body weight, body weight gains and food consumption. Fluopyram is not considered teratogenic and it induced fetal toxicity only in the presence of maternal toxicity.

In an acute oral neurotoxicity study in rats, females in all dose groups exhibited decreased session motor and locomotor activity on the day of testing. Males were similarly affected starting at the mid dose. A supplemental study with females at lower doses was able to determine a no observed adverse effect level (NOAEL) for those effects. In the short-term oral neurotoxicity test in rats, there was no evidence of neurotoxicity following dietary administration of fluopyram. Noted effects matched those in the main toxicity studies, namely, decreased food consumption and increased liver, kidney and thyroid weight.

A pyridyl-carboxylic acid metabolite of fluopyram was tested in an acute oral toxicity study and a short-term toxicity study, both in rats. In the acute study, the LD_{50} was greater than 2000 mg/kg bw with piloerection observed following the day of dosing at 500 mg/kg bw. The short-term study resulted in decreased body weight gain and food consumption. The metabolite was less toxic than parent fluopyram in the studies provided.

Results of the toxicology studies conducted on laboratory animals with fluopyram and its associated end-use products are summarized in Appendix I, Tables 2–5. The toxicology endpoints for use in the human health risk assessment are summarized in Appendix I, Table 6.

Incident Reports

Since 26 April 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 Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pesticideincident. Incident reports from Canada and the United States were searched for fluopyram and any additional information submitted by the applicant during the review process was considered. As of 13 March 2012, there were no health-related incident reports for this active in the PMRA Incident Reporting database.

3.1.1 *Pest Control Products Act* Hazard Characterization

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

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

With respect to potential prenatal and postnatal toxicity, there was no indication of increased susceptibility of fetuses or offspring compared to parental animals in the reproductive toxicity and prenatal developmental toxicity studies. In the 2-generation rat reproductive toxicity study, adverse effects on offspring body size and weight only occurred in the presence of maternal toxicity (liver, adrenal, blood and bodyweight effects). Maternal toxicity (bodyweight effects in both species and liver effects in rats) in the oral developmental toxicity studies in rats and rabbits also tempered concern for the decreased fetal weight in both species, the skeletal variations in rats and the number of runts in rabbits. Fluopyram was not considered teratogenic.

Overall, endpoints in the young were well characterized and not considered serious in nature. The *Pest Control Products Act* factor was reduced to 1-fold. The endpoints selected for risk assessment were protective of the effects noted in the rat and rabbit reproduction and developmental toxicity studies.

3.2 Acute Reference Dose (ARfD)

General Population

To estimate acute dietary risk (one day), the acute oral neurotoxicity study in rats with a NOAEL of 50 mg/kg bw was selected for risk assessment. At the lowest observed adverse effect level (LOAEL) of 100 mg/kg bw, session motor and locomotor activities were decreased in females. 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 were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. The composite assessment factor (CAF) is 100.

The ARfD is calculated according to the following formula:

$$\text{ARfD (gen. pop.)} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{50 \text{ mg/kg bw}}{100} = 0.5 \text{ mg/kg bw}$$

3.3 Acceptable Daily Intake (ADI)

To estimate dietary risk from repeat exposure, the 24-month oral chronic toxicity/oncogenicity study in rats with a NOAEL of 1.2 mg/kg bw/day was selected for risk assessment. At the LOAEL of 6.0 mg/kg bw/day, increases in liver hypertrophy, kidney weight and histopathology, cellular casts in urine, thyroid hypertrophy and colloid alteration and ocular toxicity were all observed. This study provides the lowest NOAEL in the database. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. The composite assessment factor (CAF) is 100.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{1.2 \text{ mg/kg bw/day}}{100} = 0.012 \text{ mg/kg bw/day}$$

Cancer Assessment

Fluopyram showed evidence of oncogenicity in both the rat and the mouse. There was some evidence supporting a threshold-based mechanism to the tumors (thyroid tumours in mice and liver tumours in rats), however, further data are required to establish MOAs. In the interim, a linear low dose extrapolation (Q_1*) was used for risk assessment, but is considered to be conservative. The Q_1* was set at 1.72×10^{-2} $(\text{mg/kg bw/day})^{-1}$.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Occupational and residential exposure to fluopyram is characterized as short- to long-term and is predominantly by the dermal and inhalation routes.

Short- and Intermediate-term Dermal Exposure

For short- and intermediate-term dermal risk assessment, the short-term dermal toxicity study in rats was selected. At the dose of 1000 mg/kg bw/day, clinical chemistry effects and liver toxicity were evident. A NOAEL of 300 mg/kg bw/day was established.

The target MOE selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. This MOE is considered to be protective of all adults including pregnant and lactating women and their unborn children, as well as nursing infants and children of exposed female workers.

Short- and Intermediate-term Inhalation Exposure

For short- and intermediate-term exposure via the inhalation route, the 90-day oral toxicity study in rats was selected for risk assessment. A NOAEL of 12.5 mg/kg bw/day was established based on decreased food consumption, liver and kidney toxicity and clinical chemistry alterations at 60.5 mg/kg bw/day. This study provides the lowest short- to intermediate-term toxicity NOAEL in the database. A short-term inhalation study was not available.

The target MOE for these scenarios is 100, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. This study and target MOE are considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Long-term Dermal and Inhalation Exposure

For long-term dermal and inhalation risk assessment, the 24-month oral chronic toxicity study in rats with a NOAEL of 1.2 mg/kg bw/day was selected for risk assessment. At the LOAEL of 6.0 mg/kg bw/day, increases in liver hypertrophy, kidney weight and histopathology, cellular casts in urine, thyroid hypertrophy and colloid alteration and ocular toxicity were all observed. Repeat-dose inhalation toxicity studies were not conducted and the duration of the 28-day dermal toxicity study was not appropriate for long-term exposure scenarios thus necessitating the use of an oral study for risk assessment.

The target MOE selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. This target MOE is considered to be protective of all adults including nursing infants and the unborn children of exposed female workers.

Pick-Your-Own and Residential Dermal Exposure

For the dermal risk assessment in pick-your-own and residential ornamental use scenarios, the short-term dermal toxicity study in rats was selected. At a dose of 1000 mg/kg bw/day, clinical chemistry effects and liver toxicity were evident. A NOAEL of 300 mg/kg bw/day was established.

The target MOE selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. This MOE is considered to be protective of all adults including pregnant and lactating women and their unborn children, as well as nursing infants and children of exposed women. For reasons outlined in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold.

Pick-Your-Own and Residential Oral Exposure

For the oral risk assessment in pick-your-own and residential ornamental use scenarios, the acute neurotoxicity study in rats was selected. At the doses of 100 mg/kg bw, session motor and locomotor activities were decreased in females. A NOAEL of 50 mg/kg bw was established.

The target MOE selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. This MOE is considered to be protective of all adults including pregnant and lactating women and their unborn children, as well as nursing infants and children of exposed women. For reasons outlined in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold

3.4.1.1 Dermal Absorption

An in vivo dermal absorption study in rats as well as an in vitro dermal absorption study using human and rat skin were submitted. In the in vivo rat dermal absorption study, male Wistar rats were dosed with approximately 5 or 0.005 mg/cm^2 fluopyram. Animals were exposed for an eight-hour period, after which time the skin was washed. Animals were terminated at 8, 24, 72 or 168 hours after dosing. The absorbed dose was calculated by summing residues in urine, faeces, cage wash, treated skin which had been tape stripped to remove the stratum corneum, surrounding skin, blood and carcass. The mean absorbable dose was 2.53, 4.53, 3.02 and 2.24% at the high dose and 12.81, 8.68, 10.96, and 11.76% at the low dose for the four termination periods, respectively.

An in vitro dermal penetration study with rat and human skin was conducted concurrently with the same doses used in the in vivo study. Human abdominal skin and rat dorsal skin were dosed in flow-through diffusion cells. Skin samples were exposed for 8 hours and then swabbed to remove non-absorbed dose. At the end of the study (24 hours), the skin was swabbed again, and then tape stripped. Radioactivity in the receptor fluid and the skin were combined to determine the absorbable dose. At the low dose, 14.76% of the applied dose was absorbable in rat skin and 2.95% of the applied dose was absorbable in human skin samples. From this study, human skin appears to be five times less permeable than rat skin.

The dermal absorption studies for fluopyram generally met the requirements and 'minimal standards' of the draft NAFTA triple pack approach (a combination of dermal absorption data including in vitro and in vivo data in rats and in vitro data in human). As such, it was considered appropriate to apply the 'triple pack' approach to this active ingredient. Due to uncertainties regarding in vitro reproducibility, variability in the in vitro human dermal absorption data and regional variability in human skin, the highest value of the human in vitro results (6.90%) was chosen instead of the mean value of the samples.

As a result, the dermal absorption value of 7% was selected for use in the risk assessment for fluopyram. This value may need to be reconsidered for formulations and uses other than those currently registered. For non-cancer risk estimates, a dermal absorption factor was not required, since the dermal toxicological endpoint was based on a dermal study.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to products containing fluopyram during mixing, loading and application. Exposure is expected to be of short- to intermediate-term in duration and to occur by the dermal and inhalation routes. Application is by groundboom field sprayer, airblast applicator, drip irrigation and aerial application.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted. Exposure estimates for mixers, loaders, applicators (M/L/A) are based on data from the Pesticide Handlers Exposure Database (PHED). PHED version 1.1 is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates. With a few exceptions, the PHED estimates meet criteria for data quality, specificity and quantity outlined under the North American Free Trade Agreement Technical Working Group on Pesticides. To estimate exposure for each use scenario, appropriate subsets of A and B were created from the liquid mixer/loader and groundboom, airblast or aerial applicator database files of PHED. All data were normalized for kg of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency (summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part). Inhalation exposures were based on light inhalation rates (17 LPM). The exposure estimates are based on M/L/A wearing long-sleeved shirts, long pants and chemical resistant gloves (Appendix I, Table 7).

For non-cancer exposure, the maximum application rate was combined with the unit exposures and default area treated per day values. Exposure was calculated using the following equation:

$$\text{Exposure } (\mu g/kg \text{ bw/day}) = \frac{\text{Unit Exposure } (\mu g/kg \text{ a.i. handled}) \times \text{Application Rate } (kg \text{ a.i./ha}) \times \text{Area Treated } (ha)}{\text{Body Weight } (kg)}$$

Risk of concern is based on the equation, NOAEL/exposure, where concerns are identified if the MOE is less than the target MOE. Dermal MOEs were calculated based on a NOAEL of 300 mg/kg bw/day from a 28-day rat dermal toxicity study. Inhalation MOEs were based on a NOAEL of 12.5 mg/kg bw/day from a 90-day rat oral toxicity study. The target MOE for both routes of exposure is 100. Non-cancer exposure and risk estimates for fluopyram are presented in Appendix I, Table 8. Non-cancer MOEs for all scenarios are above the target MOE.

A deterministic cancer risk assessment was conducted for farmers and custom applicators mixing/loading and applying products containing fluopyram to the approved crops. Absorbed average daily doses (ADD; equivalent to the exposure estimate for the calculations of non-cancer MOEs with a 7% dermal absorption factor) were used as the basis for calculating lifetime average daily dose (LADD) values. Dermal and inhalation ADD values were added to obtain combined ADD values. LADD values were then calculated by amortizing exposure over the lifetime of the worker based on the use pattern using the following equation.

$$\text{LADD} = \frac{\text{ADD} \times \text{Treatment Frequency} \times \text{Duration of Exposure (40 years)}}{365 \text{ days/year} \times \text{Life Expectancy (75 years)}}$$

The treatment frequency for farmers was assumed to be equal to the maximum number of applications per year for farmers and up to 60 days per year for custom applicators, since custom applicators can apply the same product on several farms. An exposure-duration of 40-years was assumed for farmers and custom applicators.

Cancer risks were calculated by multiplying an estimated LADD by a Q_1^* for fluopyram derived from the dose response data in the appropriate toxicological study [$Q_1^* = 1.72 \times 10^{-2}$ (mg/kg bw/day)$^{-1}$].

$$\text{Cancer Risk} = \text{LADD} \times Q_1^*$$

Cancer risks for farmers and custom applicators mixing/loading and applying products containing fluopyram to all approved crops are below 1×10^{-5} (Appendix I, Table 9), and are considered acceptable.

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

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

Since no chemical specific dislodgeable foliar residue (DFR) data was submitted, a default DFR value of 20% of the application rate with a 10% daily dissipation rate was used to estimate risk to workers contacting treated foliage. A tier one approach was used, in that, the highest transfer coefficient for each crop group was used to estimate exposure. Postapplication exposure was calculated using the following equation:

$$\text{Exposure } (\mu g/kg\ bw/day) = \frac{DFR \times \text{Transfer Coefficient} \times \text{Exposure Duration (8 hours)}}{\text{Body Weight (kg)}}$$

Non-cancer risks for workers entering treated fields for fluopyram are above the target MOE for all crops and activities (Appendix I, Table 10).

A deterministic cancer risk assessment was conducted for fluopyram for workers entering fields treated with fluopyram to all approved crops. ADD was used as the basis for calculating LADD values. A time weighted average DFR value over a 30-day period assuming 2 applications made 7 days apart, and assuming a dissipation rate of 10% per day was used in the calculation of ADD for workers entering treated areas. LADD values were then calculated by amortizing exposure over the lifetime of the worker based on the use pattern using the following equation.

$$LADD = \frac{ADD \times \text{Exposure Frequency} \times \text{Duration of Exposure (40 years)}}{365\ \text{days/year} \times \text{Life Expectancy (75 years)}}$$

The exposure frequency was assumed to be equivalent to 30 days for all approved crops. An exposure-duration of 40 years was assumed for re-entry workers.

Cancer risks were calculated by multiplying an estimated Lifetime LADD by a Q_1^* for fluopyram derived from the dose response data in the appropriate toxicological study [$Q_1^* = 1.72 \times 10^{-2}$ (mg/kg bw/day)$^{-1}$].

$$\text{Cancer Risk} = LADD \times Q_1^*$$

Cancer risks for worker entering fields treated with fluopyram are below 1×10^{-5} (Appendix I, Table 11) and are considered acceptable for all crops except wine grapes. For workers hand harvesting, training, thinning, hand pruning, tying and leaf pulling in grapes, a cancer risk estimate of 1.6×10^{-5} was calculated. This value was calculated with a 30-day time weighed average DFR value for grapes assuming two applications made 7 days apart (which is assumed to be the minimum re-treatment interval for grapes). This cancer risk estimate assumed postapplication exposure would occur daily for 8 hours per day, for 30 consecutive days following the first application, each year for 40 years. In addition, default DFR values (20% of the application rate) and a 10% daily dissipation rate were used to estimate cancer risk, and a preharvest interval (PHI) of 7 days is required for harvesting grapes. For these reasons, the cancer risk for grapes is expected to be a conservative estimate and is considered acceptable.

3.4.3 Residential Exposure and Risk Assessment

3.4.3.1 Handler Exposure and Risk

There are no domestic products; therefore no residential mixer/loader/applicator risk assessment is required.

3.4.3.2 Postapplication Exposure and Risk

There is potential for postapplication exposure to the general population entering areas treated with fluopyram. Since fluopyram is for use on apples and strawberries, exposure from pick-your-own (PYO) farms was considered as well as exposure to apple trees in residential areas. The postapplication risk assessment for workers is considered adequate to cover off risk to the general population picking apples and strawberries at PYO facilities and those exposed to treated residential apple trees since the duration of exposure is expected to be shorter than for commercial workers.

As there is potential for a person to be exposed through contact with treated foliage as well as eating the fruits that they are harvesting, both dermal and dietary exposure are generally aggregated in a PYO risk assessment. However, since no specific overlapping effects were noted between the dermal and oral endpoints chosen for fluopyram, an aggregate assessment for PYO scenarios was 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. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for enforcement is fluopyram in plant commodities, and fluopyram including the metabolite fluopyram-benzamide (expressed as parent equivalent) in animal commodities. The residue definition for risk assessment is fluopyram including the metabolite fluopyram-benzamide in crops of Crop Group 6 (Legume Vegetables) and 20 (Oilseeds), and fluopyram in all other plant commodities. The residue definition for risk assessment is fluopyram including the metabolites fluopyram-benzamide and fluopyram-olefines (total of 2 isomers) (expressed as parent equivalent) in poultry tissues and eggs, and fluopyram including the metabolites fluopyram-benzamide, fluopyram-olefines (total of 2 isomers) and fluopyram-7-hydroxy (expressed as parent equivalent) in ruminant tissues and milk.

The HPLC-MS/MS enforcement analytical methods are valid for the quantitation of fluopyram residues in crop matrices, and for the quantitation of fluopyram and the benzamide metabolite in livestock matrices. The residues of fluopyram and the benzamide metabolite are stable in representative matrices from five different crop categories (commodities with high water, high oil, high protein, high starch and high acid content) for up to 36 months when stored at -20°C. Therefore, fluopyram residues are considered stable in all frozen crop matrices and processed crop fractions for up to 36 months. Fluopyram residues concentrated in the following processed commodities: sugar beet refined sugar (1.3×), wheat bran (2.7×), wheat germ (2.4×), corn bran (2.6×), refined corn oil (2.6×) and refined peanut oil (1.5×). Adequate feeding studies were carried out to assess the anticipated residues in livestock matrices resulting from the currently approved uses. Supervised residue trials conducted throughout the United States and Canada using end-use products containing fluopyram in or on potatoes, sugar beets, dry beans, dry peas, soybeans, watermelon, apples, cherries, strawberries, wine grapes, almonds, pecans, wheat, sorghum, corn (field and sweet), canola, peanuts and cottonseed, and in Latin America on bananas are sufficient to support the proposed maximum residue limits (MRLs).

3.5.2 Exposure from Drinking Water

3.5.2.1 Concentrations in Drinking Water

Estimated environmental concentrations (EECs) of fluopyram 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 fluopyram in groundwater were calculated using the LEACHM model to simulate leaching through a layered soil profile over a 50-year period. The calculated concentrations using LEACHM are based on the flux, or movement, of pesticide into shallow groundwater with time. EECs of fluopyram in surface water were calculated using the PRZM/EXAMS models, which simulate pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in two types of vulnerable drinking water sources, a small reservoir and a prairie dugout.

A Level 1 drinking water assessment was conducted using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. The Level 1 EEC estimate is expected to allow for future use expansion into other crops at this application rate. Appendix I, Table 12, lists the application information and main environmental fate characteristics used in the simulations. Fifteen initial application dates for surface water, and six initial application dates for groundwater modelling between late April and late July were modelled. The models were run for 50 years for all scenarios. The largest EECs of all selected runs are reported in Appendix I, Table 13.

The EECs for chronic refined dietary exposure assessment were not acceptable. The highest EECs for Level 1 were from the dugout scenario, and hence, it was decided to model region specific crops relevant for dugout use only (Prairie region). There were two main runs for Level 2 which reflected two different intervals for application timing, and also two different crops and regions. The first was two applications of 250 g a.i./ha each at a 7-day interval (for example, watermelon) and the second was with the same applications at a 14-day interval (for example, peanut, almond). The largest Level 2 EECs for the dugout are reported in Appendix I, Table 13.

Since some toxicological data is uncertain and is undergoing further investigation, an attempt was made to estimate risks by modelling the use of fluopyram for one, two, or three years of applications. For surface water, these limited applications were tested on Saskatchewan and Prince Edward Island scenarios. For dugout modelling, the use pattern and date of application were the same as in Level 2 (2×250 g a.i./ha at a 14-day interval). For reservoir modelling, PEI-potato was run with the use pattern modeled at Level 1 (2×250 g a.i./ha at a 7-day interval). The application date selected for the runs was the date giving the highest EEC in Level 1 modelling. For groundwater, the use pattern was the same as in Level 1 (2×250 g a.i./ha at a 7-day interval). For each restricted use pattern, the LEACHM model was run 12 times each with fluopyram applied starting in one of the first twelve years of the simulation. This gave 12 different EEC's for each case. In addition the aerobic soil metabolism half-life was recalculated by taking the 80^{th} percentile of a lognormal distribution fitted to the seven available values. Results for the additional Level 2 modeling are summarized in Appendix I, Table 14.

For the ground water restricted applications, further analysis was performed for consideration of chronic effects by providing EECs averaged over 5, 10, 20 and 70 year periods. These are shown in Appendix I, Table 15, together with the daily and yearly EECs. EECs for all eleven groundwater scenarios have been provided to allow for consideration of crops restrictions. Also for information purposes, the numbers of days when EECs exceed 2 µg/L for each of the eleven scenarios are provided in Appendix I, Table 16.

Additional Level 2 modelling was conducted for groundwater. A reduced potato use rate at yearly application of 400 g a.i./ha (two applications of 150 g a.i./ha plus one of 100 g a.i./ha at the interval of 7 days) for three consecutive years application only and 100 years of consecutive application was modelled for groundwater. The groundwater EECs averaged over 70 years are reported in Appendix I, Table 17, for the three and 100 consecutive years of application.

3.5.3 Dietary Risk Assessment

Acute and chronic (cancer and non-cancer) dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), 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

The following criteria were applied to the refined chronic non-cancer analysis: Supervised trial mean residue (STMR) values, experimental processing factors, where available, Canadian and American projected percent crop treated values, and anticipated residues for livestock commodities. The refined chronic dietary exposure from all supported fluopyram food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 7% of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to fluopyram from food and water is 19.6% (0.002350 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for infants less than one year old at 63.8% (0.007661 mg/kg bw/day) of the ADI.

The refined cancer risk assessment was conducted based on a limited three-year application period and with the same criteria used for the chronic non-cancer assessment. The lifetime cancer risk from exposure to fluopyram in food and water is estimated to be 1×10^{-6} for the general population, which is considered acceptable.

3.5.3.2 Acute Dietary Exposure Results and Characterization

The following criteria were applied to the basic acute analysis: 100% crop treated, default processing factors, and residues of fluopyram in/on crop and animal commodities at MRL levels. The basic acute dietary exposure from all supported fluopyram food uses was estimated to be 4.4% of the ARfD for the general population (95^{th} percentile, deterministic). Aggregate exposure from food and water is considered acceptable and below PMRA's level of concern. Specifically, an acute dietary exposure of 2.8% to 9.8% of the ARfD was obtained for all population subgroups, with children 1-2 years old as the highest exposed population subgroup.

3.5.4 Aggregate Exposure and Risk

The aggregate risk for fluopyram consists of exposure from food and drinking water sources only. Given that apples and strawberries can be treated with fluopyram, there is potential for exposure to fluopyram during pick-your-own harvesting activities and during harvesting of fruit from trees, in residential settings, that may have been treated. Since the acute dietary and short-term dermal toxicological endpoints are based on different toxicological effects, no aggregation of dermal and dietary exposure is required.

3.5.5 Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Wine grapes	2.0
Canola	1.8
Crop Group 15 (except rice) – Cereal Grains, except rice; Cherries; Strawberries	1.5
Bananas; Watermelon	1.0
Dry chickpeas and dry lentils	0.4
Apples	0.3
Sugar beet roots; Dry soybeans	0.1
Grain lupin, dry kidney beans, dry lima beans, dry navy beans, dry pink beans, dry pinto beans, dry tepary beans, dry beans, dry adzuki beans, dry blackeyed peas, dry catjang seed, dry cowpea seed, dry moth beans, dry mung beans, dry rice beans, dry southern peas, dry urd beans, dry broad beans, dry guar seed, dry lablab beans	0.09
Crop Group 14 – Tree Nuts Group	0.05
Crop Subgroup 1C – Tuberous and Corm Vegetables Subgroup; Peanuts	0.02
Undelinted cotton seeds	0.01
Meat byproducts of cattle, goats, horses and sheep	0.40
Meat byproducts of poultry	0.10
Eggs; Milk	0.06
Fat and meat of cattle, goats, horses and sheep	0.05
Meat byproducts of hogs; Fat and meat of poultry	0.03
Fat and meat of hogs	0.02

MRLs are proposed for each commodity included in the listed crop groupings in accordance with the Residue Chemistry Crop Groups webpage in the Pesticides and Pest Management section of Health Canada's website.

For additional information on 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 methodologies, field trial data, and acute and chronic (cancer and non-cancer) dietary risk estimates are summarized in Appendix I, Tables 1, 18a-18h and 19.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Physico-chemical properties, fate and behaviour of fluopyram in terrestrial and aquatic systems are summarized in Appendix I, Tables 20-24.

Based on its physical and chemical properties, fluopyram is soluble in water, is not likely to volatilize from moist soil or water surfaces under field conditions, has a limited potential for phototransformation in the environment, does not dissociate under environmentally relevant pH conditions and has a potential for bioaccumulation in aquatic organisms.

Fluopyram is stable to hydrolysis, photolysis, aerobic and anaerobic biotransformation in soils. It is persistent in soils and has a potential for long-term accumulation and residue carry over to the following crop season. No major transformation products were detected in soils in laboratory and field studies under Canadian field use conditions. Minor transformation products identified in soils were fluopyram-7-hydroxy, fluopyram-pyridyl-carboxylic acid, fluopyram-benzamide and fluopyram-methyl-sulfoxide (only in laboratory studies). Fluopyram forms neither major nor minor transformation products in soils under anaerobic conditions.

Based on the laboratory adsorption studies, fluopyram is classified as moderately mobile in soils. In field studies, residues of fluopyram were detected beyond 30 cm soil depths. These studies indicate that fluopyram has a potential to leach and contaminate the groundwater depending on the soil type and location. None of the transformation products were, however, detected beyond 30 cm soil depth, which indicate that they have a low potential to leach and contaminate the groundwater. According to the bioaccumulation study with bluegill sunfish, fluopyram has a low potential for bioconcentration/bioaccumulation in organisms.

Fluopyram can enter aquatic systems through spray drift, overland runoff or through the movement of soil particles with bound residues. Photolysis is not an important route of transformation in the aquatic environment. Fluopyram is persistent in sediment/water aquatic systems under aerobic and anaerobic conditions and partitions significantly from water to the sediment. No major transformation products were detected in the water or sediment phases. Several minor transformation products were detected in natural water of which one was identified as fluopyram-lactam.

Based on relatively low vapour pressure and Henry's Law Constant, fluopyram is not expected to partition to the atmosphere.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. The 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 (that is, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify products and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. Screening level EECs in soil, water, aquatic eco-scenarios, vegetation and other food sources are presented in Appendix I, Tables 25-27 and Tables 38-39.

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

4.2.1 Risks to Terrestrial Organisms

A risk assessment of fluopyram and its associated end-use products was undertaken for terrestrial organisms based on available toxicity data for earthworms (acute and chronic), bees (acute oral and contact), predatory and/or parasitic invertebrates, birds (acute oral, dietary and chronic), mammals (acute oral, dietary and chronic) and terrestrial plants (effects on seedling emergence and vegetative vigour). A summary of terrestrial toxicity data for fluopyram is presented in Appendix I, Table 28, and the accompanying screening level risk assessment in Appendix I, Tables 29, 30, 31, 33, 34, 36, 40, 41, 43, 44, 46, 47, 48 and 50. Refined EECs and risk assessments for fluopyram with spray drift and runoff water are presented in Appendix I, Tables 32, 35, 37, 42, 45 and 49.

Earthworm

Fluopyram is not acutely toxic to earthworms. Although chronic effects (reproduction) were observed, low RQ values indicated that the LOC was not exceeded and, therefore, fluopyram will not pose a risk to earthworms.

Honey bees
No mortalities or adverse effects were observed when bees were exposed to fluopyram on an acute oral or contact basis. The low RQ values indicated that the level of concern was not exceeded and, therefore, fluopyram will not pose a risk to bees.

Parasitic wasps and predatory mites
No acute toxicity was observed in wasps and mites when exposed to fluopyram. Although chronic effects (reproduction) were observed in mites, the low RQ values indicated that the LOC was not exceeded and therefore, fluopyram will not pose a risk to parasitic wasps and predatory mites.

Wild birds and mammals
To characterize exposure, the concentration of fluopyram on various food items is used to determine the amount of pesticide in the diet, or estimated daily exposure (EDE). As exposure is dependent on the body weight of the organism and the amount and type of food consumed, a set of generic body weights is used to represent a range of species (20, 100 and 1000 g for birds, and 15, 35 and 1000 g for mammals). In addition, specialized feeding guilds are considered for each category of animal weights (herbivore, frugivore, insectivore and granivore). The EDE is calculated as follows: EDE = (FIR/bw) × EEC, where the food ingestion rate (FIR) is based on equations from Nagy (1987), bw is the generic body weight of the organism, and the EEC is the expected environmental concentration.

At the screening level, the risk is characterized only for feeding guilds associated with the most conservative exposure estimate (insectivores feeding on small insects or herbivores feeding on short grass) and it is assumed that food items are contaminated with maximum residue levels. In addition, only acute oral and reproduction endpoints are considered.

Wild birds: Fluopyram is not acutely toxic to birds. The RQ values were less than the LOC and small, medium and large birds are, therefore, not at potential risk on an acute basis.

Fluopyram adversely affects the reproductive performance of birds if the level of consumption exceeds 4.12 mg a.i./kg bw/day. Screening level risk assessment indicated that fluopyram may pose a risk to reproductive performance of small, medium and large birds.

The risk assessment for reproduction was therefore expanded to include all relevant food guilds and food items and also to include both on-field and off-field exposure scenarios with both maximum and mean nomogram residue concentrations. For off-field scenarios, a percent drift of 74, 59 and 6% was considered for early airblast, late airblast and field spray applications, respectively.

When considering even mean nomogram residues, on-field RQs exceeded the LOC for small and medium insectivores for all three end-use products, as well as for large herbivores with Luna Privilege. Off-field RQs exceeded the LOC only for airblast applications with Luna Privilege and Luna Tranquility Fungicide. The highest RQs were observed for small insectivorous birds for both on-field and off-field scenarios.

To further explore the potential for reproductive concern, a refined risk assessment was undertaken based on the LOAEL. The RQ values still exceeded the LOC for small and medium insectivorous birds with exposure to mean concentrations; these RQs, however, only marginally exceeded the LOC. Due to the conservative nature of the risk assessment, these marginal exceedances of the LOC are unlikely to result in adverse effects on reproductive performance. However, as a precautionary measure, bird toxicity label statements are required.

Wild mammals: Fluopyram is acutely non-toxic to mammals. The RQ values were less than the LOC and the small, medium and large mammals are, therefore, not at potential risk on an acute basis.

Fluopyram adversely affects the reproductive performance of mammals if the level of exposure exceeds 13.9 mg a.i./kg bw/day. The reproductive RQ values with direct exposure to contaminated food in the treated field (on-field) exceeded the LOC for medium and large sized mammals with Luna Privilege and medium sized mammals with Luna Tranquility Fungicide. The risk assessment for reproduction was, therefore, expanded to include all relevant food guilds and food items including on-field and off-field exposure scenarios with maximum and mean residue concentrations. For off-field scenarios, a percent drift of 74, 59 and 6% was considered for early airblast, late airblast and field spray applications, respectively.

Risk quotients exceeded the level of concern only for medium and large herbivores when considering exposure with maximum residue concentrations. With mean residue concentrations, the LOC was, however, not exceeded for any of the feeding guilds. Also, no reproductive risk was identified for all mammals feeding on food items contaminated from spray drift off the treated area (field spray applications).

The risk assessment was based on the conservative assumption that a mammal fed on 100% of a given food item and that all food was contaminated. Given that the LOCs were exceeded by a small margin for some but not for all food items considered in the risk assessment, the overall risk to mammals is considered to be low and that the wild mammals are likely have a diet comprised of different types of food items. To further support this conclusion, reproduction RQs were also calculated using a LOAEL. The RQ values with the LOAEL indicate that the LOC was not exceeded for both on-field and off-field exposure to maximum as well as mean residue concentrations for medium sized mammals.

As such, the risk to reproductive performance of wild mammals is expected to be limited (minimal).

Non-target terrestrial plants

Studies on toxicity/effects on seedling emergence and vegetative vigour indicated EC_{25} values of greater than 500 and 250 g a.i./ha (the highest applications rates tested), respectively. The RQ values exceeded the LOC with Luna Privilege, but not with the Luna Tranquility Fungicide and Propulse Fungicide. As such, fluopyram may affect plant growth with the approved uses of Luna Privilege.

As screening level risk assessment indicated a risk, a refined risk assessment was undertaken to assess the risk to non-target plants due to spray drift. Three application scenarios (airblast early (74% drift), airblast late (59% drift) and ground boom (6% drift) applications) were used to assess the risk to non-target plants due to spray drift.

As the RQ values indicated that the LOC was not exceeded, the approved uses of Luna Privilege will not affect the seedling emergence with all the three application scenarios. For vegetative vigour, however, the RQ value is slightly greater than one for the airblast early application scenario and, therefore, the approved uses of Luna Privilege may pose a risk to non-target terrestrial plants. Risk mitigation measures such as buffer zones are, therefore, required to protect non-target terrestrial habitats.

4.2.2 Risks to Aquatic Organisms

Aquatic organisms can be exposed to fluopyram 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 were used as exposure estimates. A risk assessment of fluopyram end-use products was undertaken for freshwater and marine aquatic organisms based on available toxicity data for 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 fluopyram is presented in Appendix I, Table 51. For acute toxicity studies, uncertainty factors of 1/2 and 1/10 $EC(LC)_{50}$ are used in modifying the toxicity values for aquatic plants and invertebrates, and fish species, respectively when calculating RQs. No uncertainty factors are applied to chronic NOEC endpoints. For groups where the LOC is exceeded (that is, RQ $\geq$ 1), a refined Tier 1 assessment is conducted to determine risk resulting from spray drift and runoff water separately. The calculated RQs are summarized in Appendix I, Tables 52 and 56 (screening level), 53 & 57 (Tier 1 runoff) and 54 and 58 (Tier 1 spray drift).

Freshwater fish
Fluopyram is acutely toxic to cold and warm water fish and also would result in chronic adverse effects at concentrations greater than 0.135 mg a.i./L. The low RQ values, however, indicate that the LOC was not exceeded and therefore, the freshwater fish are not a potential risk. Further, a bioaccumulation study with bluegill sunfish showed that fluopyram has a low potential for bioconcentration/bioaccumulation in aquatic organisms.

Amphibians
As no amphibian data were submitted, acute and chronic risk to amphibians were assessed using surrogate values of the most sensitive fish species – that is, rainbow trout and fathead minnow, respectively. The EECs for ground application were estimated for a water depth of 15 cm. The RQ values for the acute and chronic exposures exceeded the LOC, which indicate that the approved uses of fluopyram may pose acute and chronic risks to amphibians.

The Screening level risk assessment conducted was a conservative scenario of direct application into a body of water. As this assessment indicated a potential risk to amphibians, a refined risk assessment was conducted by estimating EECs in runoff water from treated areas into a receiving water body and by spray drift.

For acute risk to amphibians from runoff, the estimated peak EEC (acute exposure in a 15 cm depth water body) from the aquatic eco-scenario modelling was used to assess the acute risk. The acute LC_{50} for the most sensitive fish species, rainbow trout, was used as a surrogate for the amphibians. The RQ values indicated that the LOC was still exceeded and therefore, the approved of uses of fluopyram may pose an acute risk for amphibians from runoff.

For chronic risk to amphibians from runoff, the estimated EEC (21 day chronic exposure in a 15 cm depth water body) from the aquatic eco-scenario modelling was used for the risk assessment. The 21-day EEC was chosen to calculate the RQ as the chronic fathead minnow study period was 33 days. The chronic NOEC for fathead minnow was used as a surrogate for the amphibians. The RQ value indicated that the LOC was exceeded and the approved uses of fluopyram may pose a chronic risk for amphibians.

Three application scenarios, airblast early (74% drift), airblast late (59% drift), and ground boom (6% drift) applications were used to assess the risk to amphibians due to spraydrift. The acute and chronic RQs values indicated that the LOC was exceeded and the approved uses of fluopyram may pose an acute and chronic risk for amphibians due to spray drift from airblast early and late applications. The LOC was not exceeded for ground boom applications.

A refined risk assessment with run-off and spray drift (airblast) scenarios indicated that the approved uses of fluopyram may pose a risk to amphibians and, therefore, risk mitigation measures such as buffer zones are required to protect these organisms.

A screening level risk assessment was conducted with an EEC from direct aerial overspray with the approved application rates for potatoes. This assessment indicated that the LOC was exceeded for acute and chronic exposures and, therefore, a refined risk assessment was conducted with 23% spray drift for aerial applications (Appendix I, Table 55). This assessment indicated that the LOC was not exceeded for acute and chronic exposures for one metre off-field and, therefore, amphibians in the off-field are not at risk from the approved aerial applications for potato. A default buffer zone of one meter is, however, approved to cover uncertainty between direct overspray and one meter off field exposure.

Freshwater invertebrates

Fluopyram is acutely toxic to freshwater invertebrates (*Daphnia* sp.) and would result in adverse chronic effects if the concentrations in water exceed 1.214 mg a.i/L. The acute and chronic RQ values, however, indicated that the LOC was not exceeded and, therefore, the approved uses of fluopyram would pose a negligible risk to freshwater aquatic invertebrates.

Sediment-dwelling organisms
Fluopyram is persistent in aquatic systems and therefore, risk to sediment-dwelling organisms was also assessed. Chronic toxicity data for *C. riparius* and *C. tentans* were submitted which indicate that chronic adverse effects would result if the concentrations in sediment and pore water exceed 26.0 and 3.8 mg a.i./L, respectively. The RQ values were less than the LOC which indicated that the approved uses of fluopyram would pose a negligible risk to sediment-dwelling organisms.

Freshwater algae
Fluopyram is acutely toxic to freshwater algae and the most sensitive freshwater algal species is green algae. Low RQ values, however, indicated that the LOC was not exceeded and, therefore, the approved uses of fluopyram would pose a negligible risk to freshwater algae.

Freshwater plants
Adverse effects on aquatic plant, *Lemna gibba,* were observed when exposed to fluopyram. Low RQ values, however, indicated that the LOC was not exceeded and, therefore, the approved uses of fluopyram would pose a negligible risk to aquatic plants.

Marine fish
Fluopyram is acutely toxic to marine fish and the most sensitive species is sheepshead minnow. The RQ value, however, indicated that the LOC was not exceeded and therefore, marine fish are not at potential risk with the approved uses of fluopyram.

Marine invertebrates
Fluopyram is acutely toxic to marine invertebrates and the most sensitive species is eastern oyster. The low RQ values, however, indicated that the LOC was not exceeded and therefore, marine invertebrates are not at potential risk with the approved uses of fluopyram.

Marine algae
Fluopyram is acutely toxic to marine algae and the most sensitive species is saltwater diatom. The low RQ values, however, indicate that LOC was not exceeded and therefore, marine algae are not at potential risk with the approved uses of fluopyram.

Marine amphipods
Fluopyram is acutely toxic to marine amphipods and would result in chronic adverse effects if exposed to concentrations greater than 0.55 mg a.i./L. The low acute and chronic RQ values, however, indicated that the LOC was not exceeded and therefore, the approved uses of fluopyram would pose a negligible risk to marine amphipods.

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Acceptable Efficacy Claims

The number of submitted trials reviewed in support of the efficacy claims on the Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide labels totalled 57, 18, and 14 trials, respectively. Proposed and supported claims are listed in Appendix I, Tables 59 to 61.

5.1.1.1 Almond and cherry

Brown rot blossom blight
The same five trials were used as evidence to support the efficacy of Luna Privilege against brown rot blossom blight in both almond and cherry given the similarities between the two crops and their susceptibility to the disease. Four trials were conducted on various related species of stone fruit trees including cherry. The fifth trial was conducted on almond. Averaged across the different trials, disease severity reduction reached up to 84%. Average levels of reductions in disease incidence across the trials were somewhat lower at 61%. Although almond production in Canada is negligible, developments in almond breeding have opened the possibility of introductions of hardier types and varieties of almonds that could be used in establishing viable commercial production in Canada.

5.1.1.2 Apple

Leaf scab
Five trials conducted on apple were used to demonstrate the efficacy of Luna Privilege against leaf scab. Up to 100% control, in terms of both disease severity and incidence, was obtained on leaves of tested trees. Disease control on fruits, although more variable than on leaves, also reached levels up to 100% in certain trials. It was noted that the label claim is indicated for control of the disease specifically on the leaf, rather than the fruit. Therefore, the levels of disease control observed across the apple trials were sufficient to support the claim for control of leaf scab.

In addition, Luna Tranquility Fungicide was also shown to be highly effective against this disease. Across the nine trials where the co-formulation was tested on apple leaf scab, up to 83% control was observed when fluopyram and pyrimethanil were applied together. Applied individually, each active ingredient provided significantly lower levels of protection than the combination product. This, along with considerations related to disease resistance management, further demonstrated the value of the co-formulation.

Powdery mildew
In two trials, Luna Tranquility Fungicide provided high levels of protection and performed better than a registered standard. Control, in terms of disease severity, was reported to have reached almost 100% in the Luna Tranquility Fungicide treatment. Although pyrimethanil was shown to have limited activity against powdery mildew in apple on its own, the main benefits of the co-formulation are primarily in broadening the spectrum of diseases controlled.

5.1.1.3 Bean, dry

Powdery mildew
Direct evidence used in demonstrating Luna Privilege efficacy against powdery mildew in legume vegetables, including dry bean, was obtained from one trial conducted on peas. This evidence was supplemented by trials conducted on other crops (for example, cucurbits and wheat) where powdery mildew is caused by different but related species of pathogens. In all of these trials, Luna Privilege provided excellent protection against powdery mildew. Specifically, in the pea trial, disease severity was reduced by 81 to 100% under high disease pressure.

White mold
Across three trials on dry bean and one trial on edible bean, which was accepted as support for the dry bean claim, severity and incidence of white mold were generally reduced by over 90% in stems and pods by Luna Privilege treatments. These levels of efficacy were sufficient in demonstrating acceptable levels of white mold control in dry bean.

The combined efficacy of the two active ingredients in Propulse Fungicide was tested in six trials. Damage caused by white mold along with infection of pods and yields were assessed in the various trials. In one of the trials, reductions in the percentage of damage caused by white mold reached up to 98% under moderate to high disease pressure. Higher yields relative to the untreated control were observed in the plots treated with the co-formulation in all of the trials where yield was measured. In another trial, where the percentage of infected pods was assessed, reductions of up to 70% by Propulse Fungicide relative to the untreated control plots were observed. Overall, the product provided equivalent or superior protection to the tested standard currently registered for control of white mold in dry bean.

Ascochyta blight & mycosphaerella blight
Efficacy of Luna Privilege against ascochyta blight on dry bean was demonstrated across six field trials conducted on chickpea and lentil. In most trials, Luna Privilege was shown to be considerably more effective at reducing levels of disease severity than disease incidence. Under very high disease pressure, disease control reached up to 86% in one of the chickpea trials.

Because mycosphaerella blight is closely related to ascochyta blight and both diseases are biologically similar, the evidence described above was also deemed to be supportive of the mycosphaerella blight claim. In addition, two trials on pea directly assessing the effect of Luna Privilege on mycosphaerella blight demonstrated similarly high levels of protection under high disease pressure.

The combined effect of the two active ingredients in the co-formulated product Propulse Fungicide on ascochyta blight and mycosphaerella blight was demonstrated across eight trials on lentil, pea, and chickpea. As with fluopyram alone, the combination of two active ingredients provided excellent levels of reduction in disease severity. For instance, over 81% control of ascochyta blight was obtained in the lentil trial where the higher of the two label rates of Propulse Fungicide was applied. In five different trials conducted on chickpea, damage caused by ascochyta blight was reduced by an average of 85% and 91% when assessed 12 to 30 days after the final application of Propulse Fungicide at the low and high label rates, respectively. It was also observed that, on average, both label rates of Propulse Fungicide provided substantially higher levels of protection than the tested commercial standards in terms of disease severity and damage.

As both active ingredients in Propulse Fungicide are known to be effective on their own, either from previously registered claims or from the fluopyram trials described above, it can be concluded that this product provides added benefits in terms of resistance management.

5.1.1.4 Cherry

Powdery mildew
Two trials were conducted to demonstrate the efficacy of Luna Privilege against powdery mildew on cherry. Under heavy infestation, applications of the product at the lower labelled rate provided 62% reductions in disease. However, under moderate disease pressure and at the higher labelled rate, disease control reached 94% relative to the untreated control treatment. As described for other crops appearing on the label, Luna Privilege also has demonstrated excellent efficacy against a number of other powdery mildew-causing organisms.

5.1.1.5 Grape, wine

Powdery mildew
The efficacy of the combination product Luna Tranquility Fungicide was tested in four trials. Under moderate to high disease pressure, the product provided consistently high levels of control. Reductions in disease severity and incidence both reached 100% in many instances. Although the efficacy of fluopyram alone was not tested directly in these trials, it was indirectly demonstrated by observations where the combination of fluopyram and pyrimethanil provided 100% control where pyrimethanil alone provided a maximum of 36% control under high disease pressure. In light of demonstrated efficacy for both components, the combination product offers the benefit of simultaneous applications of multiple modes of fungicide action that are effective, thereby reducing the risk of resistance development.

Botrytis bunch rot/Grey mold
Across four trials conducted on grape, Luna Privilege provided excellent levels of protection against botrytis bunch rot. Control, in terms of disease severity, ranged from 83-99% and was shown to be equivalent to currently registered standards under moderate and high disease pressure. Reductions of disease incidence were also high, ranging from 58-92%. As efficacy of fluopyram applied alone was demonstrated in these trials and pyrimethanil, as the lone active ingredient of Scala SC Fungicide, is already registered for the control of botrytis bunch rot, the combination product Luna Tranquility Fungicide is expected to provide dual effective modes of action against botrytis bunch rot and reduce the risk of resistance development.

5.1.1.6 Peanut

Early and late leaf spot
Luna Privilege showed excellent levels of early leaf spot control in three field trials conducted on peanut. Control, in terms of disease incidence and severity, reached 89% and 96%, respectively. On the other hand, the product's efficacy against late leaf spot was demonstrated in two other field trials. In these, incidence and severity of late leaf spot were both reduced by more than 80%.

5.1.1.7 Potato

Early blight
Luna Privilege provided excellent levels of early blight control across four trials conducted on potato. Under moderate to high disease pressure, early blight severity and incidence was reduced by up to 90% and 100%, respectively. In addition, aerial applications were shown to be equally as effective as ground applications of Luna Privilege.

5.1.1.8 Strawberry

Powdery mildew
A total of six trials were conducted to demonstrate the efficacy of Luna Privilege in reducing powdery mildew in strawberry. Only applications by chemigation appear on the label. Luna Privilege provided high levels of efficacy against powdery mildew when applied to strawberry. The labelled rate of Luna Privilege provided average reductions of disease severity and incidence across the three chemigation trials of around 72% and 70%, respectively. Maximum levels of disease reduction reached 82% and 93% for severity and incidence of powdery mildew, respectively.

5.1.1.9 Watermelon

Powdery mildew
Thirteen trials demonstrating efficacy on two different species of powdery mildew-causing organisms conducted on a variety of cucurbit crops (pumpkin, squash, melon, cucumber, and zucchini) were reviewed as evidence for this claim. This set of data provided excellent support for Luna Privilege efficacy against both species of powdery mildew. The highest reductions in disease severity across the trials ranged from 81-100%, all under at least moderate, and often high disease pressure.

Botrytis grey mold
In trials conducted on other crops (grape and strawberry), high levels of protection by Luna Privilege were demonstrated against the same pathogen that causes grey mold in cucurbits. Because of the similarities in grey mold susceptibility shared among the tested crops and cucurbits, the results of these trials were extrapolated as evidence to support this claim on watermelon.

5.2 Phytotoxicity

Observations of crop tolerance to Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide, were reported in a total of 61, 23, and 16 submitted field trials, respectively. Phytotoxicity was not observed from any of the three products when applied at rates consistent with their labelled use patterns.

5.3 Economics

No market analysis was done for this submission.

5.4 Sustainability

5.4.1 Survey of Alternatives

The chemical and other non-conventional/biological fungicidal active ingredients listed in Appendix I, Table 62, are found in products that are registered for control or suppression of diseases indicated on the Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide labels.

5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

The use of fluopyram products should be integrated into a disease management program to attenuate the probability of resistance development to fungicides that have a similar mode of action. Integrated pest management (IPM) promotes the integration of cultural, biological, mechanical and chemical control strategies. Proper use of IPM aims to reduce pesticide use while maintaining economic returns through effective pest control and maximum crop production. Fluopyram fungicides represent one component of the chemical strategy for disease control. The use of fluopyram will complement other disease management strategies in the supported crops.

The addition of fluopyram as another chemical control option will potentially increase the longevity of other products with different modes of action as viable options for specific disease control. Combining chemical control with other cultural or biological control measures should minimize the dependence on any one control measure and therefore minimize the potential for resistance or increased tolerance to develop to any one control measure.

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

Fungicides in the succinate dehydrogenase inhibitors group, such as fluopyram, are considered to present a medium to high risk of disease resistance development by Fungicide Resistance Action Committee. Resistance to this group of fungicides has been observed for several fungal species in field populations and lab mutants. Among cases of field resistance reported by Fungicide Resistance Action Committee that are specifically relevant to the uses registered on the three fluopyram-containing product labels are resistant field isolates of powdery mildew in cucurbits and botrytis in various hosts. In addition, suspected resistant isolates of *Sclerotinia sclerotiorum*, the pathogen that causes white mold on bean and other legumes, were found in European rape seed fields.

5.4.4 Contribution to Risk Reduction and Sustainability

Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide are safe on labelled crops and fit well into current IPM strategies when used according to directions. These broad spectrum products will benefit fruit and vegetable producers and offer a useful alternative in disease resistance management. In addition, because Luna Tranquility Fungicide and Propulse Fungicide each combine two active ingredients with different modes of action, the risk of disease resistance development is reduced in targeted pathogens that are sensitive to the two active ingredients.

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: in other words, 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, fluopyram and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[4] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Fluopyram does not meet all Track 1 criteria, and is not considered a Track 1 substance. (Appendix I, Table 63)
- Fluopyram does not form any transformation products that meet all Track 1 criteria.

Technical grade fluopyram and its associated end-use products do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.[5]

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

[5] DIR2006-02, Formulants Policy and Implementation Guidance Document.

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 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, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

The end-use products have, as a component, the preservative 1,2-benzisothiazoline-3-one (0.015%), which contains low levels of polychlorinated dibenzodioxins and furans (TSMP Track 1). As the use of this preservative was recently re-evaluated and found to be acceptable, and because the input of dioxins into the environment from pesticides is being managed as outlined in the PMRA Regulatory Directive DIR99-03 for the implementation of TSMP, the Agency position is that no further action is required.

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

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for fluopyram 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. While motor/locomotor activity were decreased in the neurotoxicity study, fluopyram is not believed to be selectively neurotoxic. In short-term and chronic studies on laboratory animals, the primary targets were the liver, thyroid and kidneys. Although fluopyram was not genotoxic, there was evidence of oncogenicity in mice and rats after chronic dosing. 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.

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

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

The nature of the residues in plants and animals is adequately understood. The residue definition for enforcement is fluopyram in plant products and fluopyram including the metabolite fluopyram-benzamide in animal matrices. The approved uses of fluopyram on watermelon, wine grapes, strawberries, dry beans, dry chickpeas, dry lentils, peanuts, apples, potatoes, cherries and almonds 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 MRLs (see Table 3.5.1).

Mixers, loaders and applicators handling products containing fluopyram and workers re-entering treated areas are not expected to be exposed to levels of fluopyram that will result in risks of concern when the products are used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

Residential exposure to individuals contacting treated fruits or foliage is not expected to result in risks of concern when products containing fluopyram are used according to label directions.

7.2 Environmental Risk

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

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

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

Fluopyram presents a negligible risk to soil organisms, bees, beneficial arthropods, freshwater and marine fish, invertebrates, algae and aquatic plants. Fluopyram, however, may pose a risk to non-target terrestrial plants from spray drift (Luna Privilege only), and to amphibians due to runoff and spray drift. In order to minimize the potential risk, no-spray buffer zones between the treated area and downwind sensitive terrestrial and aquatic habitats are required. A bird toxicity label statement is also required as a precaution.

7.3 Value

The information submitted to register Luna Privilege, Luna Tranquility Fungicide, and Propulse Fungicide adequately demonstrated the value of the products in the management of a broad spectrum of foliar diseases and other fungal pathogens on various vegetable and fruit crops.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, has granted a conditional registration for the sale and use of the technical active, Fluopyram Technical Fungicide and end-use products, Luna Privilege containing the technical grade active ingredient fluopyram, Luna Tranquility Fungicide containing the technical grade active ingredients fluopyram and pyrimethanil and Propulse Fungicide containing the technical grade active ingredients fluopyram and prothioconazole to control various fungal diseases on various horticultural and field crops.

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

Although the risks and value have been found acceptable when all risk-reduction measures are followed, as a condition of these registrations, additional scientific information (listed below) is being requested from the applicant as a result of this evaluation. For more details, refer to the Section 12 Notice associated with these conditional registrations.

NOTE: The PMRA will publish a consultation document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

Human Health

- DACO 4.3.1 – Short term mode of action studies addressing the observed tumours. The goal of these studies is to further inform the two proposed cancer modes of action.
- DACO 7.2.3 (Inter-Laboratory Analytical Methodology Validation) – An independent laboratory validation of Method GM-001-P07-01 for the determination of fluopyram residues in plant matrices is required to fulfill the data requirement for an acceptable enforcement method in plant matrices.
- DACO 7.4.4 (Field Accumulation Studies) – A full set of field rotational crop data are required for canola, soybean and cereals (wheat, barley and corn, both field and sweet).

Value

- One field trial to confirm the efficacy of Luna Privilege against powdery mildew on standard sized cherry trees.
- One field trial to confirm efficacy of Luna Privilege against late leaf spot on peanuts.

List of Abbreviations

µg	micrograms
AB	Alberta
AD	administered dose
ADD	absorbed daily dose
ADI	acceptable daily intake
A:G	albumin/globulin
a.i.	active ingredient
ALAT	alanine aminotransferase
ALK	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
ASAT	aspartate amino-transferase
BAF	bioaccumulation factor
BC	British Columbia
BCF	bioconcentration factor
BROD	benzyloxyresorufin *O*-deethylation
BW/bw	body weight
bwg	body weight gain
CAF	composite assessment factor
CAS	Chemical Abstracts Service
cm	centimetres
cm^2	centimetres square
cm^3	cubic centimetres
CO_2	carbon dioxide
d	day(s)
DFOP	Double-First-Order in Parallel
DFR	dislodgeable foliar residue
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{75}	dissipation time 75% (the time required to observe a 75% decline in concentration)
DT_{90}	dissipation time 90% (the time required to observe a 90% decline in concentration)
dw	dry weight
EC_{05}	effective concentration on 5% of the population
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
ER_{50}	effective rate on 50% of the population
EROD	7-ethoxyresorufin *O*-deethylation
F_1	first generation
F_2	second generation
FC	food consumption
FIR	food ingestion rate

fw	fresh weight
g	gram
GGT	gamma glutamyltransferase
GIT	gastrointestinal tract
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
HDPE	high-density polyethylene
HPLC	high performance liquid chromatography
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
IBC	intermediate bulk container
IPM	integrated pest management
IUPAC	International Union of Pure and Applied Chemistry
K_d	soil-water partition coefficient
kg	kilogram
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	litre
LADD	lifetime average daily dose
LC_{50}	lethal concentration 50%
LD	low dose
LD_{50}	lethal dose 50%
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOQ	limit of quantitation
LPM	litre per minute
LR_{50}	lethal rate 50%
m	metre(s)
m^3	cubic metre
MAS	maximum average score
MB	Manitoba
mg	milligram
MIS	maximum irritation score
mL	millilitre
M/L/A	mixer/loader/applicator
MOA	mode of action
MOE	margin of exposure
mol	mole
MRL	maximum residue limit
MTD	maximum tolerated dose
N/A	not applicable
N/R	not required
NAFTA	North American Free Trade Agreement
NC	not classified
nm	nanometre(s)
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level

NOEC	no observed effect concentration
NR	not reported
NS	Nova Scotia
NZW	New Zealand white
ON	Ontario
Pa	Pascal
PBI	plantback interval
PCA	Fluopyram-pyridyl-carboxylic acid
PEI	Prince Edward Island
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
PROD	pentoxyresorufin *O*-deethylation
PYO	pick-your-own
Q1*	cancer potency factor
QC	Quebec
RA	risk assessment
RBC	red blood cell
ROLD	repeat oral low dose
RQ	risk quotient
SFO	single-first-order
SK	Saskatchewan
SOHD	single oral high dose
SOLD	single oral low dose
STMdR	supervised trial median residue
STMR	supervised trial mean residue
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSH	thyroid stimulating hormone
TSMP	Toxic Substances Management Policy
TWA	time weighted average
UDP	uridine diphosphate
US	United States
UV	ultraviolet
wk	week(s)

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	Limit of Quantitation		PMRA #
Soil	01068	fluopyram	HPLC-MS/MS	1 µg/kg in soil		1599625
Soil	00973 01023	fluopyram	HPLC-MS/MS	1 µg/kg in soil		1599622
		AE C656948-benzamide (AE148815)				
		AE C656948-7-hydroxy (BCS-AA-10065)				
		AE C656948-PCA				
Soil/ Sediment	GM-002-S07-01 GM-002-S07-04	fluopyram	HPLC-MS/MS	1 µg/kg in soil and sediment		1599627
		AE C656948-benzamide (AE148815)				
		AE C656948-7-hydroxy (BCS-AA-10065)				
		AE C656948-PCA				
Water	01051	fluopyram	HPLC-MS/MS	0.05 µg/L in drinking and surface water		1599623
Plant	GM-001-P07-01 enforcement method	fluopyram	HPLC-MS/MS	0.01 ppm	grape, strawberry, tomato	1599619
	00984	fluopyram, AE C656948-benzamide, AE C656948-pyridyl-carboxylic acid, AE C656948-pyridyl-acetic acid, AE C656948-7-hydroxy and AE C656948-methyl-sulfoxide		0.01 ppm for each analyte (except AE C656948-pyridyl-carboxylic acid on rape seed and AE C656948-methyl-sulfoxide on rape seed, wheat grain and lettuce)	lettuce head, rape seed, wheat grain, and orange	1599621
				0.05 ppm for each analyte (except AE C656948-methyl-sulfoxide)	wheat straw	
	modification M001 to 00984	fluopyram, AE C656948-benzamide, AE C656948-pyridyl-carboxylic acid, AE C656948-pyridyl-acetic acid		0.01 ppm	processed commodities of apple, tomato, cabbage, grape, rape seed and strawberry	1599793, 1599737
Animal	01079 enforcement method	fluopyram and AE C656948-benzamide	HPLC-MS/MS	0.01 ppm	eggs, milk, fat, liver, kidney, muscle	1599626, 1599769
	Method 01061	Fluopyram, AE C656948-benzamide, AE C656948-olefine (E- and Z- isomers)		0.01 ppm for fluopyram and AE C656948-benzamide; 0.02 ppm for calculated total residue of AE C656948-olefine (E- and Z- isomers)	eggs, milk, cream, fat, liver, kidney, muscle	1599624

Table 2 Toxicity Profile of Luna Privilege
(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	Study Results	PMRA #
Acute oral toxicity Wistar rats	Female LD_{50} > 2000 mg/kg bw Low toxicity	1599335
Acute dermal toxicity Wistar rats	LD_{50} > 2000 mg/kg bw Low toxicity	1599336
Acute inhalation toxicity (nose-only) Wistar rats	LC_{50} > 2.09 mg/L Low toxicity	1599337
Dermal irritation NZW rabbits	MAS = 0, MIS = 0 Non-irritating	1599338
Eye irritation NZW rabbits	MAS = 0, MIS = 5.3 Minimally irritating	1520933
Dermal sensitization (LLNA) CBA/J mouse	Non-sensitizer	1599340

Table 3 Toxicity Profile of Luna Tranquility 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	Study Results	PMRA #
Acute oral toxicity Sprague Dawley rats	Female LD_{50} > 5000 mg/kg bw Low toxicity	1670082
Acute dermal toxicity Wistar rats	LD_{50} > 2000 mg/kg bw Low toxicity	1670083
Acute inhalation toxicity (nose-only) Wistar rats	$LC_{50} \geq$ 2.0 mg/L Low toxicity	1670084
Dermal irritation NZW rabbits	MAS = 0, MIS = 0 Non-irritating	1670085
Eye irritation NZW rabbits	MAS = 0, MIS = 2 Non-irritating	1670086
Dermal sensitization (LLNA) CBA/J mouse	Non-sensitizer	1670087

Table 4 Toxicity Profile of Propulse 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	Study Results	PMRA #
Acute oral toxicity Sprague Dawley rats	Female LD_{50}: >5000 mg/kg bw Low toxicity	1670748
Acute dermal toxicity Sprague Dawley rats	LD_{50}: >5050 mg/kg bw Low toxicity	1670747
Acute inhalation toxicity (nose-only) Wistar rats	LC_{50}: ≥2.2 mg/L Low toxicity	1670744

Study Type/Animal	Study Results	PMRA #
Dermal irritation NZW rabbits	MAS = 0, MIS = 0 Non-irritating	1670745
Eye irritation NZW rabbits	MAS = 0, MIS = 0 Non-irritating	1670746
Dermal sensitization (Buehler) Guinea pigs	Non-sensitizer	1670749

Table 5 Toxicity Profile of Technical Fluopyram 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. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted)

Study Type/Animal	Study Results	PMRA #
Metabolism/ toxicokinetics (single and repeat dose, oral, gavage) Wistar rat	**Rate and extent of absorption and excretion:** Fluopyram was rapidly and effectively absorbed (93-98% of total recovered radioactivity; ♂), as determined in a low dose (LD) bile-cannulation study. The AUC indicated slightly higher systemic exposure for females than males in the single oral low dose (SOLD; 5 mg/kg bw) tests and proportionality according to the dose. These findings were confirmed by quantitative whole body autoradiography. Toxicokinetic data indicated major differences based on the part of the molecule that had been radiolabelled. Time to maximum plasma concentrations with the phenyl label were reached at 15 h in males and 11 h in females (t_{max}) in SOLD animals, while that for repeat oral low dose (ROLD; 5 mg/kg bw/d – unradiolabelled for 14 d with radiolabelled fluopyram on day 15) animals was faster (0.8 h). The study with the pyridyl label produced much shorter t_{max} values of 0.7 h and 3.3 h for SOLD males and females, respectively. The C_{max} of single oral high dose of the phenyl label (SOHD; 250 mg/kg bw; phenyl) animals was between 35-42 h, suggesting delayed absorption with increasing dose. There was evidence of an initial elimination phase of 10-11 h, followed by a slower terminal elimination phase of 56-73 h with a SOLD of the pyridyl label. The majority of faecal and urinary excretion occurred within the first 72-96 hours; however, there was evidence of continuing excretion beyond 168 h as evidenced by radioactive residues remaining in the carcass at sacrifice and the confirmatory autoradiography results. Routes of excretion varied depending on the location of the radiolabel. In males, faecal excretion accounted for approx. 53% administered dose (AD), while urinary excretion ranged from 38-45% AD. In females treated with the phenyl label, there were virtually equal proportions of fluopyram excreted via the faeces and urine; in contrast, 39% AD was faecal and 60% AD was urinary with the pyridyl label. Bile-cannulated males showed total excretion of 90-100% AD, primarily due to biliary excretion within the first 24 h, suggesting extensive enterohepatic circulation. There were no significant levels of radiolabeled fluopyram in expired air. **Distribution / target organ(s):** Fluopyram was rapidly and widely distributed in the body. The highest radioactive residues were observed in the liver, kidney and Harderian gland, and in some studies, in the carcass, RBC, ovaries, thyroid and adrenal glands. Total radioactivity remaining in the carcass was 2-6% AD for the phenyl label and 0.3-0.5% AD for the pyridyl label. There was some evidence of retention of fluopyram at 168 hours, particularly via the renal route. No subsequent time-points were examined and thus the possibility of bioaccumulation could not be excluded. **Toxicologically significant compound(s):** Fluopyram was extensively	1599513, 1599517, 1599524, 1599526, 1599529

Study Type/Animal	Study Results	PMRA #
	metabolized, with the ethyl linking group of the parent as the preferred site for metabolism, resulting in 7-hydroxy and 8-hydroxy metabolites. Further oxidation resulted in -enol, which was further conjugated to glucuronic acid. Hydroxylation of the phenyl ring resulted in –phenol and 7-OH-phenol metabolites. Elimination of water from compounds hydroxylated in the ethylene bridge resulted in fluopyram-Z-olefine and E-olefine metabolites (E- and Z-olefine can isomerize into each other). As the double bond of olefine may be a target for epoxidation and a dihydroxy-metabolite (which could result from hydrolysis of an epoxid by epoxid hydrolase) was observed, the olefine was considered to be of potential toxicological significance. All of the hydroxylated metabolites were conjugated primarily to glucuronic acid and to a lesser extent with sulfate. The cleavage of the molecule yielded label-specific metabolites (-benzamide; -pyridyl-acetic acid, -ethyl-diol, -pyridyl carboxylic acid) that represented the most abundant metabolites. This molecule was further metabolized via oxidation, hydroxylation and conjugation. The phenyl ring moiety was also conjugated with glutathione followed by further degradation to 7-OH-methyl-sulfone, -BA-methyl-sulfoxide and -BA-methyl-sulfone (phenyl label only). There were apparent sex differences in the quantity of metabolites generated. Fluopyram-7-hydroxy wand 7-OH-phenol metabolites were higher in males than females. Females showed higher amounts of 8-hydroxy and -benzamide than males. Low dose females excreted more of phenyl specific -benzamide and -benzoic acid than males. Females treated with the pyridyl label excreted more –pyridyl-acetic acid than males, while males excreted more –ethyl-diol metabolites than females. Parent accounted for 0.4/1.9% AD ♂/♀ for the SOLD group and 10.5/16.7% AD ♂/♀ for the SOHD group. Biliary metabolites were likely formed after first pass, with subsequent conjugation in GIT and subsequent excretion in faeces. There were no significant differences in metabolism between the doses, or between single and repeat dosing.	
Acute oral toxicity Wistar rats	Female LD_{50}: >2000 mg/kg bw Low Toxicity	1599564
Acute dermal toxicity Wistar rats	LD_{50}: >2000 mg/kg bw Low Toxicity	1599563
Acute inhalation toxicity (nose-only) Wistar rats	LC_{50}: >5.1 mg/L air Low Toxicity	1599559
Skin irritation NZW rabbits	MAS = 0, MIS = 0 Non-irritating	1599561
Eye Irritation NZW rabbits	MAS = 1.8, MIS = 8. 7 Minimally irritating	1599558
Skin Sensitization (LLNA) CBA/J mice	Non-sensitizer	1599573
4-week dermal toxicity Wistar rat	Systemic NOAEL = 300 mg/kg bw/day Dermal NOAEL = 1000 mg/kg bw/day 1000 mg/kg bw/day: ↑ prothrombin time, ↑ cholesterol, ↑ liver weights, ↑ minimal centrilobular and mid-zonal hepatocellular hypertrophy No treatment-related dermal effects.	1599533
28-day dietary C57BL/6J mouse	Range-finding 24.7/31.1 mg/kg bw/day ♂/♀: ↑ liver weights, ↑ centrilobular hepatocellular hypertrophy	1599579

Study Type/Animal	Study Results	PMRA #
	162/197 mg/kg bw/day ♂/♀: ↑ liver weights, ↑ enlarged & dark livers, ↑ centrilobular hypertrophy, ↑ focal necrosis in liver; ↑ single cell hepatocellular necrosis ♂; ↑ hypertrophy of zona fasciculata in adrenals ♀ 747/954 mg/kg bw/day ♂/♀ (exceeded MTD): ↑ mortality due to intrathoracic hemorrhage, sacrificed Days 17-27, preceded by severe clinical signs (↓ motor activity, hunched, piloerection, wasted appearance, cold to touch, laboured respiration, distended abdomen), marked bw loss, ↓ fc, ↑ pale pancreas, rounded borders in liver, dark & enlarged livers, reduced thymic size, distended abdomen, adrenal hypertrophy, vacuolation, degeneration/necrosis of zona fasciculate, perivascular & intra-alveolar hemorrhage of lungs, degeneration of pulmonary veins, erythroid extramedullary hematopoiesis in spleen, ↓ cellularity & focal hemorrhage, thyroid, centrilobular hypertrophy of hepatocytes, hepatocyte eosinophilia, bile duct/oval cell hyperplasia, focal necrosis, single cell necrosis; red liquid thoracic cavity, centrilobular degeneration/necrosis ♂ Surviving females: Distended abdomen, ↑ total cholesterol, total protein, ↑ ALAT, ↑ enlarged & dark livers, ↑ hypertrophy of zona fasciculata in adrenals, ↑ centrilobular hypertrophy in liver, ↑ single cell hepatocellular necrosis, ↑ focal necrosis in liver, ↑ hepatocellular eosinophilia, ↑ bile duct/oval cell hyperplasia	
28-day dietary Wistar rat	Range-finding ≥31.0/36.1 mg/kg bw/day ♂/♀: ↑ liver weights, ↑ enlarged, dark livers with prominent lobulation, ↑ centrilobular hepatocellular hypertrophy, ↑ pale kidneys, ↑ basophilic tubules, hyaline droplets in proximal tubule, granular casts in medulla, ↑ P450, BROD, PROD; ↑ thyroid weights, ↑ kidney weights ♂ 254/263 mg/kg bw/day ♂/♀: ↓ bwg, ↑ total cholesterol, ↑ TG, ↑ follicular hypertrophy in thyroid, slight ↑ spleen weights; ↑ colloidal depletion in thyroid, ↑ platelets, ↑ prothrombin time, ↑ size/cellularity follicles in spleen, ↑ diffuse hypertrophy pituitary basophils ♂, ↓ glucose; ↓ FC ♀	1599574
28-day gavage Beagle dog	Supplemental 750 mg/kg bw/day: ↑ Soft/liquid/no feces, ↑ ALK, ↓ albumin and albumin globulin ratio, ↑ GGT, ↑ TG, ↑ enlarged livers ↑ liver weights, ↑ centrilobular-panlobular hepatocellular hypertrophy, ↑ eosinophilic inclusions bodies; ↓ RBC, ↓ haemoglobin, ↓ hematocrit ♂	1599578
90-day dietary C57BL/6J mouse	NOAEL = 26.6/32.0 mg/kg bw/day ♂/♀ 188/216 mg/kg bw/day ♂/♀: ↑ ALAT, ↑ ALK, ↑ ASAT, ↓ albumin, ↑ adrenal weight, ↑ dark livers, ↑ focal necrosis in liver, ↑ cortical vacuolation in adrenals, ↓ cortical ceroid pigment in adrenals	1599556
90-day dietary Wistar rat	NOAEL = 12.5/14.6 mg/kg bw/day ♂/♀ ≥60.5/70.1 mg/kg bw/day ♂/♀: ↓ bilirubin, ↑ TSH, ↑ T3, ↑ T4, pale kidneys, dark livers, ↑ prominent lobulation in liver, positive cysts cortico-medullary junction, ↑ positive	1599557

Study Type/Animal	Study Results	PMRA #
	cells/debris medulla of kidney, ↑ follicular cell hypertrophy in thyroid ♂; ↓ FC,↑ diffuse centrilobular hepatocellular hypertrophy, ↑ cholesterol ♀	
90-day dietary Dog	NOAEL = 28.5/32.9 mg/kg bw/day ♂/♀ ≥171/184 mg/kg bw/day ♂/♀: ↓ bw, ↓ bwg; ↑ ALK, ↓ total bilirubin, ↓ albumin, ↓ A:G, ↓ total protein, ↑ liver weights, ↑ enlarged livers, ↑ hepatocellular hypertrophy & intracytoplasmic eosinophilic droplets; ↓ FC, ↑ hepatocellular single cell necrosis, ↑ incomplete maturation of prostate, zona glomerulosa vacuolation in adrenals ♂	1599555
12-month dietary Beagle dog	NOAEL = 13.2/14.4 mg/kg bw/day ♂/♀ 67.6/66.1 mg/kg bw/day ♂/♀: ↓ bwg wk 1, ↓ FC, ↑ ALK, ↑ GGT; ↑ diffuse hypertrophy of follicular epithelium of thyroid, ↑ diffuse centrilobular hepatocellular hypertrophy ♂; ↑ thyroid weights ♀	1599548
2-year dietary, chronic toxicity / oncogenicity (*combined*) Wistar rat	Chronic toxicity: NOAEL = 1.2/1.7 mg/kg bw/day ♂/♀ Liver carcinoma and adenoma ♀ 52-week sacrifice: 6.0/8.6 mg/kg bw/day ♂/♀: ↑ liver centrilobular to panlobular hypertrophy, ↑ kidney weight, ↑ kidney, histopathology (focal/multifocal chronic progressive nephropathy, hyaline droplets in proximal tubules), ↑ cellular casts in urine, ↑ diffuse thyroid follicular cell hypertrophy ♂ Main group: 6.0/8.6 mg/kg bw/day ♂/♀: ↑ liver weight, ↑ liver histopathology (centrilobular to panlobular hypertrophy, altered hepatocyte foci), ↑enlarged kidney, ↑ kidney histopathology (chronic progressive nephropathy, focal/multifocal tubular hyperplasia, focal/multifocal tubular dilatation, focal/multifocal tubular hypertrophy), ↑ thyroid follicular cell hypertrophy, ↑ corneal opacity, corneal oedema, nuclear opacity of lens, small retinal vessels ♂; colloid alteration ♀	1599635
18 month dietary, chronic toxicity / oncogenicity (*combined*) C57BL/6J mouse	Chronic toxicity: NOAEL = 4.2/5.3 mg/kg bw/day ♂/♀ Thyroid follicular cell adenoma ♂ 52-week sacrifice: 20.9/26.8 mg/kg bw/day (♂/♀): ↑ liver weight; ↑ enlarged liver, ↑ focal/multifocal thyroid follicular cell hyperplasia ♂ Main group: 20.9/26.8 mg/kg bw/day (♂/♀): ↑ liver weight, ↑ diffuse centrilobular to panlobular hypertrophy, ↑ focal/multifocal thyroid follicular cell hyperplasia; ↑ focal/multifocal hepatocellular single cell necrosis, ↑ platelets ♂; ↑ enlarged liver ♀	1599632

Study Type/Animal	Study Results	PMRA #
One-generation dietary (range-finding) Wistar rat Supplemental	Supplemental Parental effects ≥49.6/57.7 mg/kg bw/day ♂/♀: ↑ liver weights; ↑ kidney weight ♂ 102.1/118.2 mg/kg bw/day ♂/♀: ↓ thymus weight; ↓ premating bwg ♀	1599823
Multi-generation dietary Wistar rat	Parental NOAEL = 13.9/16.8 mg/kg bw/day ♂/♀ Reproductive NOAEL = 82.4/95.6 mg/kg bw/day ♂/♀ Offspring NOAEL = 13.9/16.8 mg/kg bw/day ♂/♀ Parental effects 82.4/95.6 mg/kg bw/day ♂/♀: ↑ centrilobular hepatocellular hypertrophy; ↑ protein droplet nephropathy and lymphocytic infiltration, ↑ cytoplasmic vacuolization in adrenals F_1, ↑ kidney weights F_0 & F_1 ♂; ↓ bw premating & gestation F_0, ↓ bwg premating F_0 & F_1, ↑ cholesterol F_1, ↑ WBC F_1, ↑ monocyte absolute cell counts F_1, ↑ liver weights F_0 & F_1, ↓ spleen weights F_0 & F_1, ↑ alveolar macrophages in lungs F_1 ♀ Offspring effects 82.4/95.6 mg/kg bw/day ♂/♀: ↓ bw F_1 & F_2, ↓ bwg F_1 & F_2, ↓ spleen and thymus weights F_2	1599824
Developmental toxicity Sprague Dawley rat	Maternal NOAEL = 30 mg/kg bw/day Developmental NOAEL = 150 mg/kg bw/day Maternal effects: ≥150 mg/kg bw/day: ↓ bwg, ↓ corrected bwg to gravid uterine weight, ↓ FC, ↑ abs. liver weight, ↑ centrilobular hepatocellular hypertrophy Developmental effects: 450 mg/kg bw/day: ↓ fetal weights, ↑ thymic remnant present, ↑ skeletal variations No evidence of teratogenicity	1599610
Developmental toxicity NZW rabbit	Maternal NOAEL = 25 mg/kg bw/day Developmental effects NOAEL = 25 mg/kg bw/day Maternal effects: 75 mg/kg bw/day: ↓ bw, ↓ bwg, ↓ corrected bwg to gravid uterine weight, ↓ FC Developmental effects: 75 mg/kg bw/day: ↓ fetal weights, ↑ runts (bw < 28.0 g)	1599571

Study Type/Animal	Study Results	PMRA #
Acute Neurotoxicity Wistar rat	Main study: NOAEL = 125 mg/kg bw/not established ♂/♀ Supplemental study (female only): Female NOAEL = 50 mg/kg bw Main study: ≥125 mg/kg bw: ↓ session motor activity, ↓ session locomotor activity ♀ ≥ 500 mg/kg bw: ↓ session motor activity, ↓ session locomotor activity ♂; ↓ body temperature, ↓ vocalization during removal ♀ Supplemental: 100 mg/kg bw: ↓ session motor activity, ↓ session locomotor activity ♀	1599618
Subchronic Neurotoxicity Wistar rat	Systemic toxicity: NOAEL = 33.2/41.2 mg/kg bw/day ♂/♀ 164.2/197.1 mg/kg bw/day ♂/♀: ↓ bw, ↓ bwg, ↑ cholesterol, ↑ bilateral retinal degeneration; ↓ FC ♂; ↑ TG, ↑ thyroid weights ♀	1599534
Gene mutations in bacteria in vitro	Negative	1599580
Gene mutations in bacteria in vitro	Negative	1599553
In vitro mammalian clastogenicity Chromosome aberrations	Negative	1599552
In vitro mammalian cell assay V79/HPRT forward mutation	Negative	1229493
In vivo cytogenetics Micronucleus assay	Negative	1229494
3-day toxicity study in male C57BL/6J mouse – pharmacokinetic investigations of the clearance of intravenous (iv)-administered ^{125}I-thyroxine	Non-guideline Whole blood thyroxine levels were lower in fluopyram-treated males at all time-points compared to controls. Similar effects were observed in PB-treated males, although the decreases from controls were marginally less and there was some evidence of recovery at 24 h.	1654272
3-day toxicity study in male C57BL/6J mice - QPCR investigations of gene transcripts in the liver	Non-guideline Fluopyram (300 mg/kg bw/day): ↑ liver weight, ↑ expression of the following genes: Cyp1a, Cyp2b, Cyp 3a, Sult1a1, Sult 2a2, Suln, Ugt1a1, Ugt2b1, Ugt2b5 PB (80 mg/kg bw): Reduced motor activity ↑ liver weight, ↑ expression of the following genes: Cyp2b, Cyp 3a, Sult1a1, Sult 2a2, Suln, Ugt1a1, Ugt2b1, Ugt2b5	1654273

Study Type/Animal	Study Results	PMRA #
3-day, 14-day toxicity in male C57BL/6J mice (dietary) – hepatotoxicity and thyroid hormones fluopyram vs. phenobarbital	Non-guideline 3 day exposure 308 mg/kg bw/day: ↓ FC, ↓ T4, ↑ TSH, ↑ liver weight, ↑ enlarged livers, ↑ centrilobular to panlobular hepatocellular hypertrophy (diffuse; graded minimal-slight), ↑ number of mitoses present, ↑ hepatocellular single cell necrosis, ↑ total P450, EROD, PROD, BROD Phenobarbital at 80 mg/kg bw/day: bw loss, ↓ FC, ↓ T4, ↓ T3, ↑ rel. liver weight, ↑ enlarged and dark livers, ↑ centrilobular to panlobular hepatocellular hypertrophy (diffuse; graded minimal-slight), ↑ number of mitoses present, ↑ total P450, EROD, PROD, BROD 14 day exposure 314 mg/kg bw/day: ↓ FC, ↓ T4, ↑ TSH, ↑ liver weight, ↑ enlarged and dark livers, ↑ centrilobular to panlobular hepatocellular hypertrophy (diffuse; graded slight-moderate), ↑ hepatocellular single cell necrosis, ↑ total P450, EROD, PROD, BROD Phenobarbital at 80 mg/kg bw/day: bw loss, ↓ FC, ↓ T4, ↑ TSH, ↑ liver weight, ↑ enlarged and dark livers, ↑ centrilobular to panlobular hepatocellular hypertrophy (diffuse; graded slight-moderate), ↑ hepatocellular single cell necrosis, ↑ total P450, EROD, PROD, BROD	1599576, 1599803
7-day toxicity in female Wistar rats (dietary) fluopyram vs. phenobarbital	Non-guideline 193 mg/kg bw/day: ↓ FC, ↑ liver weight, ↑ enlarged and dark livers, ↑ centrilobular to panlobular hepatocellular hypertrophy (diffuse; graded minimal-slight), ↓ diffuse mainly periportal hepatocellular vacuolation, ↑ BrdU labelling index in centrilobular and periportal zones of liver, ↑ total P450, EROD, PROD, BROD, UDPGT Phenobarbital at 80 mg/kg bw/day: Reduced motor activity, ↓ bw, ↓ bwg, ↑ liver weight, ↑ enlarged and dark livers, ↑ centrilobular to panlobular hepatocellular hypertrophy (diffuse; graded minimal-slight), ↑ hepatocellular necrotic focus, ↑ BrdU labelling index in centrilobular and periportal zones of liver, ↑ total P450, EROD, PROD, BROD, UDPGT	1599741, 1599802
In vitro studies with hog thyroid microsomes on the potential interactions with thyroid peroxidase-catalyzed reactions	Non-guideline Fluopyram does not affect thyroid hormone synthesis at the level of TPO under the study conditions tested. The effects of fluopyram metabolites were not studied.	1599551
METABOLITE – AE C656948-pyridyl-carboxylic acid (AE 657188)		
Acute oral toxicity Wistar rats	Female LD_{50}:>2000 mg/kg bw Low Toxicity	1599809
28-day dietary Sprague Dawley rat	NOAEL = 1574/162 mg/kg bw/day ♂/♀ 1581 mg/kg bw/day ♀: ↓ bwg, FC	1599612

Study Type/Animal	Study Results	PMRA #
Bacterial mutation assay	Negative	1599630
In vitro mammalian cell forward mutation assay	Precipitation observed at ≥4000 µg/mL in the absence of S9 mix and at 5000 µg/mL in the presence of S9 mix (data were not interpretable). Negative	1599613
Chromosome aberrations	Negative	1599611

Table 6 Toxicology Endpoints for Use in Health Risk Assessment for Fluopyram

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary general population	Rat acute neurotoxicity study	NOAEL = 50 mg/kg bw Reduced motor and locomotor activity	100
	Acute reference dose = 0.5 mg/kg bw		
Repeated dietary	Rat chronic toxicity/carcinogenicity study	NOAEL = 1.2 mg/kg bw/day Numerous effects, primarily in liver, kidney, thyroid and eye	100
	Acceptable daily intake = 0.012 mg/kg bw/day		
Short- and intermediate term dermal[2]	Rat 28 day dermal toxicity study	NOAEL = 300 mg/kg bw/day Clinical chemistry and liver effects	100
Long-term dermal[2]	Rat chronic toxicity/carcinogenicity study	NOAEL = 1.2 mg/kg bw/day Numerous effects, primarily in liver, kidney, thyroid and eye	100
Short- and intermediate-term inhalation[3]	Rat 90 day oral toxicity study	NOAEL = 12.5 mg/kg bw/day Numerous effects	100
Long-term inhalation[3]	Rat chronic toxicity/carcinogenicity study	NOAEL = 1.2 mg/kg bw/day Numerous effects, primarily in liver, kidney, thyroid and eye	100
Pick-your-own and residential ornamental oral	Rat acute neurotoxicity study	NOAEL = 50 mg/kg bw Reduced motor and locomotor activity	100
Pick-your-own and residential dermal	Rat 28 day dermal toxicity study	NOAEL = 300 mg/kg bw/day Clinical chemistry and liver effects	100
Cancer	**Q_1*** set at 1.72×10^{-2} $(mg/kg\ bw/day)^{-1}$		

[1] CAF (composite assessment factor) refers to a total of uncertainty and *Pest Control Products Act* factors for dietary assessments; MOE refers to a target MOE for occupational and residential assessments

[2] Since an oral NOAEL was selected, a dermal absorption factor was used in a route-to-route extrapolation

[3] Since an oral NOAEL was selected, an inhalation absorption factor was used in route-to-route extrapolation.

Table 7 Exposure Estimates for Mixers/Loaders/Applicators

Scenario	Area Treated per Day ha		Unit Exposure µg/kg a.i. handled		
	Non-Cancer	Cancer	Dermal	Inhalation	Combined
Groundboom- Fruits and Vegetables Farmer/Custom	26	12	84.12	2.56	86.68
Groundboom Farmer – large field crops	107	60	84.12	2.56	86.68
Groundboom Custom – large field crops	360	240	84.12	2.56	86.68
Airblast	20	7	879.38	7.4	886.78
Drip Application Mix/Load	26	12	51.14	1.6	52.74
Aerial Mix/Load	400	318	51.14	1.6	52.74
Aerial Applicator	400	318	9.66	0.07	9.73

Table 8 Non-Cancer Exposure and Risk Estimates for Mixer/Loader/Applicators Handling Fluopyram

Crop	Application Equipment	Maximum Rate kg a.i./ha	Dermal Exposure mg/kg bw/day	Inhalation Exposure mg/kg bw/day	Dermal MOE[a]	Inhalation MOE[a]
Watermelon	groundboom	0.25	0.00781	0.000238	38407	52584
Wine Grapes	airblast	0.25	0.0628	0.000529	4776	23649
Dry beans	groundboom farmer	0.15	0.0193	0.000587	15554	21296
	groundboom custom	0.15	0.0649	0.00198	4623	6330
Peanuts	groundboom	0.25	0.0321	0.000978	9332	12777
Apples	airblast	0.15	0.0377	0.000317	7960	39414
Potatoes	groundboom farmer	0.15	0.0193	0.000587	15554	21296
	groundboom custom	0.15	0.0649	0.00198	4623	6330
	aerial M/L	0.15	0.0438	0.00137	6844	9115
	aerial applicator	0.15	0.00828	0.00006	36232	208333
Strawberries	drip irrigation	0.25	0.004749	0.000149	63175	84135
Cherries	airblast	0.125	0.0314	0.000264	9552	47297
Almonds (tree nuts)	airblast	0.25	0.0628	0.000529	4776	23649

[a] Target MOE = 100

Table 9 Cancer Exposure and Risk Estimates for Mixer/Loader/Applicators Handling Fluopyram

Crop	Application Equipment	Maximum Appln Rate kg a.i./ha	Maximum Number of Apps/season	Dermal Exposure mg/kg bw/day	Inhalation Exposure mg/kg bw/day	LADD mg/kg bw/day	Cancer Risk
Watermelon	groundboom	0.25	2	0.000252	0.00011	1.06E-06	1.82E-08
Wine Grapes	airblast	0.25	2	0.001539	0.000185	5.04E-06	8.67E-08
Dry beans	groundboom farmer	0.15	2	0.000757	0.000329	3.17E-06	5.46E-08
	groundboom custom	0.15	60	0.003028	0.001317	3.81E-04	6.55E-06
Peanuts	groundboom	0.25	2	0.001262	0.000549	5.29E-06	9.10E-08
Apples	airblast	0.15	3	0.000923	0.000111	4.53E-06	7.80E-08
Potatoes	groundboom farmer	0.15	2	0.000757	0.000329	3.17E-06	5.46E-08
	groundboom custom	0.15	60	0.003028	0.001317	3.81E-04	6.55E-06
	aerial M/L	0.15	2	0.002439	0.00109	3.09E-04	5.32E-06
	aerial applicator	0.15	2	0.000461	4.77E-05	4.46E-05	7.67E-07
Strawberries	drip irrigation	0.25	2	0.000153	6.86E-05	6.49E-07	1.12E-08
Cherries	airblast	0.125	3	0.000769	9.25E-05	3.78E-06	6.50E-08
Almonds (tree nuts)	airblast	0.25	2	0.001539	0.000185	5.04E-06	8.67E-08

Table 10 Non-Cancer Postapplication Exposure and Risk Estimates for Fluopyram

Crop	Reentry Activity	Maximum Appln Rate kg a.i./ha	Max Number of Apps/season	Transfer Coefficient cm^2/h	DFR Value $\mu g/cm^2$	Dermal Exposure mg/kg bw/day	Dermal MOE[a]
Watermelon	hand harvesting, leaf pulling, hand pruning, thinning, turning	0.25	2	2500	0.7391	0.211	1421
Wine Grapes	hand harvesting, training, thinning, hand pruning, tying, leaf pulling	0.25	2	8500	0.7391	0.718	418
Dry beans	scouting, irrigation	0.15	2	1500	0.4435	0.076	3946
	hand harvesting (green peas)	0.15	2	2500	0.4435	0.127	2368
Peanuts	scouting, irrigation	0.25	2	1500	0.6144	0.105	2848
Apples	thinning	0.15	3	3000	0.5121	0.176	1709
Potatoes	scouting, irrigation	0.15	2	1500	0.4435	0.076	3946
	hand harvest (sweet potatoes)	0.15	2	2500	0.4435	0.127	2368
Strawberries	hand harvesting, thinning, hand pruning, tying, training	0.25	2	1500	0.7952	0.136	2201
Cherries	thinning	0.125	3	3000	0.4268	0.146	2050
Almonds (tree nuts)	harvesting	0.25	2	200	0.6144	0.014	21362

[a] Target MOE = 100

Table 11 Cancer Postapplication Exposure and Risk Estimates for Fluopyram

Crop	Reentry Activity	Maximum Appln Rate kg a.i./ha	Exposure Frequency days/year	30 day TWA DFR Value $\mu g/cm^2$	ADD mg/kg bw/day	LADD	Cancer Risk
Watermelon	hand harvesting, leaf pulling, hand pruning, thinning, turning	0.25	30	0.317	0.00634	0.000278	4.8E-06
Wine Grapes	hand harvesting, training, thinning, hand pruning, tying, leaf pulling	0.25	30	0.317	0.02156	0.000945	1.6E-05
Dry beans	scouting, irrigation	0.15	30	0.190	0.00228	0.000100	1.7E-06
	hand harvesting (green peas)	0.15	30	0.190	0.00380	0.000167	2.9E-06
Peanuts	scouting, irrigation	0.25	30	0.295	0.00354	0.000155	2.7E-06
Apples	thinning	0.15	30	0.273	0.00655	0.000287	4.9E-06
Potatoes	scouting, irrigation	0.15	30	0.190	0.00228	0.000100	1.7E-06
	hand harvest (sweet potatoes)	0.15	30	0.190	0.00380	0.000167	2.9E-06
Strawberries	hand harvesting, thinning, hand pruning, tying, training	0.25	30	0.322	0.00386	0.000169	2.9E-06
Cherries	thinning	0.125	30	0.227	0.00546	0.000239	4.1E-06
Almonds (tree nuts)	harvesting	0.25	30	0.295	0.00047	0.000021	3.6E-07

Table 12 Major Groundwater and Surface Water Model Inputs for Level 1, Level 2 and Level 2 Restricted Application Assessments

Type of Input	Parameter	Value
Application information: Level 1	Crop(s) to be treated	grapes, apples, water melon, wine grapes, dry beans, peanut, potato, cherry, and tree nuts
	Maximum allowable application rate per year (g a.i./ha)	500
	Maximum rate for each application (g a.i./ha)	250
	Maximum number of applications per year	2
	Minimum interval between applications (days)	7
	Method of application	Airblast
Application information: Level 2 (Dugout only)	Crops to be treated	1) grapes 2) potato (drinking water only)
	Maximum allowable application rate per year (g a.i/ha)	500
	Maximum rate each application (g a.i./ha)	250
	Maximum number of applications per year	2
	Minimum interval between applications (days)	1) 7-days 2) 14-days (drinking water)
	Method of application	Ground
Environmental fate characteristics	Hydrolysis half-life at pH 7 (days)	Stable
	Photolysis half-life in water (days)	Stable
	Adsorption K_{oc} (mL/g)	284 (20th percentile of five K_{oc} values for fluopyram)
	Aerobic soil biotransformation half-life (days)	654 for Level 1 and Level 2 (80th percentile of half-life values; values for the two labels were averaged) 533 at Level 2 restricted application (80th percentile of fitted lognormal distribution; values for the two labels were averaged)
	Aerobic aquatic biotransformation half-life (days)	1330 (longest of two half-lives; values for the two labels were averaged)
	Anaerobic aquatic biotransformation half-life (days)	1495 (single half-life; values for the two labels were averaged)

Table 13 Level 1 and Level 2 Estimated Environmental Concentrations of Fluopyram in Potential Drinking Water Sources

Compound	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)			
			Reservoir		Dugout	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[3]	Yearly[4]
Fluopyram, Level 1	106	104	26	7.8	236	231
Fluopyram, Level 2	N/A	N/A	N/A	N/A	185	181

Notes:
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
N/A = not applicable

Table 14 Level 2 Additional Modelling - Restricted Application Estimated Environmental Concentrations of Fluopyram in Potential Drinking Water Sources

Use pattern	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)			
			Reservoir		Dugout	
	Daily[3]	Yearly[4]	Daily[1]	Yearly[2]	Daily[1]	Yearly[2]
Apply one year only	15	15	17	NR	13	12
Apply two years only	28	28	26	NR	22	21
Apply three years only	40	40	26	NR	26	25

Notes: 1 90th percentile of yearly peak concentrations,
2 90th percentile of yearly average concentrations
3 90th percentile of maximum daily concentration for each of twelve starting years
4 90th percentile of maximum yearly concentration for each of twelve starting years
N/A For level 2, the reservoir and groundwater were not modelled.
N/R The yearly values were not reported as EECs would decline rapidly after the number of years of application, whether 1, 2 or 3 years. In other words, there is only one peak for each year of application and concentration declines to almost zero in subsequent years. Therefore, the 90th percentile of yearly averages calculated for these restricted years

Table 15 Groundwater EECs (µg/L) Averaged over Five Time Periods*

N years	AB_ North	AB_S_ irr	BC_F irr	BC_O_ irr	SK_ Rgina	MB_ Wnpeg	ON_ Essex	ON_ Niaga	QC_ Yamsk	PEI_ Char	NS_ Fundy
Highest daily EEC											
1	7	14.7	8	8.6	0.5	2.5	6.5	4.4	0.8	6.2	10.6
2	13.9	28.3	14.5	16.4	0.8	4.7	13.5	8.9	1.6	11.9	20.1
3	20.7	40.4	19.1	23.3	1.1	6.8	20.1	13.2	2.4	17.5	28.3
Highest one year average value											
1	6.9	14.7	7.8	8.5	0.5	2.5	6.4	4.4	0.8	6.1	10.5
2	13.6	28.2	14.1	16.4	0.7	4.7	13.2	8.8	1.6	11.8	19.8
3	20.4	40.2	18.6	23.2	1	6.8	20	13.1	2.4	17.2	27.7
Five year average EEC											
1	6.7	12.1	4.5	7.9	0.4	2.4	5.8	3.9	0.8	5.4	8.6
2	13.4	23.9	8.8	15.2	0.7	4.6	11.8	7.8	1.5	10.5	17
3	20	34.8	12.7	21.5	0.9	6.6	17.4	11.9	2.4	15.3	24.2
Ten year average EEC											
1	6.6	8.1	2.3	6.2	0.3	2.3	4.4	3.2	0.7	3.9	6
2	13	16.3	4.6	11.9	0.6	4.3	9.1	6.4	1.4	7.7	11.7
3	19.4	24.4	6.9	17.4	0.8	6.3	13.6	9.7	2.2	11.2	17
Twenty year average EEC											
1	5.6	4.4	1.2	3.9	0.3	1.9	2.6	2.1	0.6	2.2	3.2
2	11.2	8.9	2.4	7.4	0.4	3.5	5.4	4.3	1.2	4.4	6.3
3	16.6	13.4	3.6	10.7	0.5	5	8.1	6.4	1.8	6.5	9.3
Seventy year average EEC											
1	1.95	1.19	0.33	1.07	0.08	0.65	0.72	0.62	0.19	0.61	0.88
2	3.86	2.44	0.66	2.05	0.14	1.22	1.48	1.24	0.37	1.21	1.74
3	5.77	3.68	0.99	2.96	0.18	1.76	2.23	1.87	0.57	1.78	2.55

*daily, one year, five years, ten years and twenty years and seventy years - 500 g a.i./ha (two applications at 250 g a.i./ha per year)

Table 16 Number of Days When EECs Exceed 2 µg/L for All 11 Groundwater Scenarios, Assuming Applications over One, Two or Three Years

N years	AB_ North	AB_S_ irr	BC_F_i rr	BC_O_ irr	SK_ Rgina	MB_ Wnpeg	ON_ Essex	ON_ Niaga	QC_ Yamsk	PEI_ Char	NS_ Fundy
1	9297	6671	1435	4379	0	3384	3630	3332	0	3155	3190
2	11739	8063	1879	5465	0	6404	4768	5109	0	4083	3865
3	12997	8964	2263	6179	0	8114	5198	5877	2928	4696	4323

Table 17 Groundwater EECs (µg/L)* Averaged over Seventy Years

N years*	AB_ North	AB_S_ Irr	BC_F_ irr	BC_O_ irr	SK_ Rgina	MB_ Wnpeg	ON_ Essex	ON_ Niaga	QC_ Yamsk	PEI_ Char	NS_ Fundy
3	4.61	2.93	0.79	2.37	0.14	1.41	1.78	1.50	0.46	1.43	2.04
100	81	59	19	61	0.53	30	42	38	11	36	42

*averaged over 70 years assuming three or 100 consecutive years of application of fluopyram at a reduced potato use rate of 400 g a.i./ha per year (two applications of 150 g a.i./ha plus one of 100 g a.i./ha at an interval of 7 days)

Table 18a Nature of the Residues in Plant Matrices

Nature of the Residue in Grapes		**PMRA# 1599785 and 1599786**	
Radiolabeled Position	[phenyl-UL-14C] fluopyram and [pyridyl-2,6-14C] fluopyram		
Test Site	Plants were grown under natural sunlight and temperatures, except that a glass roof was automatically closed at the beginning of rainfall.		
Treatment	Three foliar spray applications at 100, 200 and 200 g a.i./ha; intervals between applications were 42 and 49 days.		
Rate	504 g a.i./ha (phenyl) and 498 g a.i./ha (pyridyl)		
End-use Product	Fluopyram 500 SC		
Preharvest interval	18 days		
Matrix	**PHI (days)**	**[phenyl-14C] TRRs (ppm)**	**[pyridyl-14C] TRRs (ppm)**
Summer Cut	After second application	28.55	64.18
Grapes	18	1.86	1.70
Leaves	19	48.06	42.66
Metabolites Identified	Major Metabolites (>10% of the TRRs)	Minor Metabolites (<10% of the TRRs)	
[phenyl-14C]			
Summer Cut	Fluopyram	None	
Grapes	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy	
Leaves	Fluopyram	AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy	
[pyridyl-14C]			
Summer Cut	Fluopyram	AE C656948-pyridyl-carboxylic acid AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy	
Grapes	Fluopyram	AE C656948-pyridyl-carboxylic acid AE C656948-7-hydroxy	

Leaves	Fluopyram	AE C656948-pyridyl-carboxylic acid AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy

Metabolism of fluopyram was rather limited in grapevine and none of the metabolites was detected at more than 1.0% of the TRRs. The main reactions involved are:
Hydroxylation of fluopyram leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy
Conjugation of AE C656948-7-hydroxy
Cleavage of hydroxylated active substance leading to AE C656948-benzamide and AE C656948-carboxylic acid

Nature of the Residue in Potatoes		**PMRA# 1599781 and 1599789**
Radiolabeled Position	[phenyl-UL-14C] fluopyram and [pyridyl-2,6-14C] fluopyram	
Test Site	Plants were grown under natural sunlight and temperatures, except that a glass roof was automatically closed at the beginning of rainfall.	
Treatment	Three foliar spray applications at approximately 167 g a.i./ha; intervals between applications were 16 and 11 days.	
Rate	518.8 g a.i./ha (phenyl) and 505.7 g a.i./ha (pyridyl)	
End-use Product	Fluopyram 500 SC	
Preharvest interval	51 days	

Matrix	**PHI (days)**	**[phenyl-14C] TRRs (ppm)**	**[pyridyl-14C] TRRs (ppm)**
Potato tuber	51	0.008	0.012
Potato leaves	51	47.64	21.67

Metabolites Identified	Major Metabolites (>10% of the TRRs)	Minor Metabolites (<10% of the TRRs)
[phenyl-14C]		
Potato tuber	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy
Potato leaves	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy
[pyridyl-14C]		
Potato tuber	Fluopyram AE C656948-pyridyl-carboxylic acid (49.8% of the TRRs; 0.006 ppm)	AE C656948-pyridyl-carboxylic acid AE C656948-7-hydroxy
Potato leaves	Fluopyram	AE C656948-pyridyl-carboxylic acid AE C656948-7-hydroxy

The metabolic pathway of fluopyram in potatoes consisted of hydroxylation of fluopyram leading to AE C656948-7-hydroxy, which is cleaved to AE C656948-benzamide and AE C656948-PCA.

Nature of the Residue in Beans		**PMRA # 1599779 and 1599787**
Radiolabeled Position	[phenyl-UL-14C] fluopyram and [pyridyl-2,6-14C] fluopyram	
Test Site	Plants were grown under natural sunlight and temperatures, except that a glass roof was automatically closed at the beginning of rainfall.	
Treatment	Two foliar spray applications at approximately 250 g a.i./ha; the interval between applications was 28 days.	
Rate	528 g a.i./ha (phenyl) and 519 g a.i./ha (pyridyl)	
End-use Product	Fluopyram 500 SC	
Preharvest interval	4 days for immature crops and 29 days for mature crops	

Matrix	**PHI (days)**	**[phenyl-14C] TRRs (ppm)**	**[pyridyl-14C] TRRs (ppm)**
Green bean	4	1.40	3.88
Foliage	4	36.66	38.53
Succulent bean	29	0.07	0.17
Dry beans	29 + drying for 11 days	0.12	0.31
Straw	29	16.55	19.02

Metabolites Identified	Major Metabolites (>10% of the TRRs)	Minor Metabolites (<10% of the TRRs)
[phenyl-14C]		

Green bean	Fluopyram	None
Foliage	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
Succulent beans	Fluopyram AE C656948-benzamide (51.9% of the TRRs; 0.036 ppm)	AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
Dry beans	Fluopyram AE C656948-benzamide (64.0% of the TRRs; 0.077 ppm)	AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
Straw	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
[pyridyl-14C]		
Green bean	Fluopyram	None
Foliage	Fluopyram	AE C656948-PCA AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
Succulent beans	AE C656948-PAA (29.5% of the TRRs; 0.051 ppm) AE C656948-PCA (31.0% of the TRRs; 0.054 ppm)	Fluopyram AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
Dry beans	AE C656948-PAA (22.6% of the TRRs; 0.070 ppm) AE C656948-PCA (32.5% of the TRRs; 0.100 ppm)	Fluopyram AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
Straw	Fluopyram	AE C656948-PCA AE C656948-PAA AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy
The main reactions of fluopyram metabolism in the beans are: Hydroxylation of fluopyram leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy Conjugation of AE C656948-7-hydroxy with glucose and malonic acid, in one case conjugation of AE C656948-8-hydroxy with glycoside and glucuronic acid Cleavage of hydroxylated active substance leading to AE C656948-benzamide and AE C656948-carboxylic acid		
Nature of the Residue in Red Bell Peppers		**PMRA# 1599782 and 1599790**
Radiolabeled Position	[phenyl-UL-14C] fluopyram and [pyridyl-2,6-14C] fluopyram	
Test Site	Soil-less cultivation (stone wool substrate) in a greenhouse	
Treatment	Drip irrigation	
Rate	A single application done at a rate of 5 mg a.i./plant. Additionally, an experiment was conducted at an exaggerated rate (4x) of 20 mg a.i./plant.	
End-use Product	Fluopyram 500 SC	

Preharvest interval	Intermediate plant (4x experiment, 33 days) Mature peppers (1x experiment, both radiolabels, three time points ranging from 55 to 96 days) Mature peppers (4x experiment, pyridyl radiolabel only, three time points ranging from 55 to 96 days) Rest of plant (1x experiment, 97 days)		
Matrix	**PHI (days)**	**[phenyl-14C] TRRs (ppm)**	**[pyridyl-14C] TRRs (ppm)**
Pepper Intermediate (4x)	33	6.237	18.24
Mature peppers (1x)	55-96	0.038	0.060
Mature peppers (4x)	55-96	Not applicable	0.149
Rest of plant (1x)	97	3.54	2.344
Metabolites Identified	Major Metabolites (>10% of the TRRs)	Minor Metabolites (<10% of the TRRs)	
[phenyl-14C]			
Intermediate plant	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy	
Mature peppers (1x)	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy glucoside conjugate of AE C656948-7-hydroxy	
Rest of plant	Fluopyram AE C656948-benzamide (10.1% of the TRRs; 0.36 ppm)	AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside and malonic acid conjugates of AE C656948-7-hydroxy	
[pyridyl-14C]			
Intermediate plant	Fluopyram	AE C656948-PCA AE C656948-7-hydroxy AE C656948-8-hydroxy glucoside conjugate of AE C656948-7-hydroxy di-glucoside conjugate of AE C656948-hydroxyethyl AE C656948-N-oxide	
Mature peppers (4x)	Fluopyram AE C656948-PCA (19.5% of the TRRs; 0.029 ppm) AE C656948-PAA-glycoside [12.5% (isomer 1) and 19.7% (isomer 2) of the TRRs; 0.019 and 0.029 ppm]	AE C656948-PAA AE C656948-7-hydroxy	
Mature peppers (1x)	Fluopyram AE C656948-PCA (43.5% of the TRRs; 0.026 ppm) AE C656948-PAA-glycoside [23.8% (isomer 1) and 14.2% (isomer 2) of the TRRs; 0.014 and 0.009 ppm]	None	
Rest of plant	Fluopyram	AE C656948-7-hydroxy glucoside conjugate of AE C656948-7-hydroxy di-glucoside conjugate of AE C656948-hydroxyethyl AE C656948-N-oxide	

The main reactions of fluopyram metabolism in the beans are:
Hydroxylation of fluopyram leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy
Conjugation of AE C656948-7-hydroxy with glucose and malonic acid
Cleavage of hydroxylated active substance leading to AE C656948-benzamide and AE C656948-carboxylic acid

Supplemental Cell Culture Study – Apple	**PMRA# 1599640**

The metabolism of fluopyram was investigated in heterotrophic plant cell suspension cultures from apple fruit following incubation with [phenyl-UL-14C] and [pyridyl-2,6-14C] fluopyram, to facilitate metabolite identification and to produce radiolabeled reference compounds for the identification of metabolites in metabolism studies. Nine metabolites (AE C656948-deschloro-3-OH-glc; AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc; AE C656948-8-hydroxy-glc; AE C656948-hydroxymethyl-benzamide; AE C656948-benzamide; AE C656948-pyridyl-hydroxyethyl; AE C656948-pyridyl-hydroxymethyl; and AE C656948-pyridyl-carboxylic acid (PCA)) were isolated and identified, which served as reference compounds for the plant and animal metabolism studies.

Proposed Metabolism in Plants
Metabolism studies conducted in four diverse crops (pepper, grapes, beans and potato) showed similar metabolic profiles, with fluopyram as a major compound in all crops. In pepper (pyridyl), potato tuber (pyridyl) and beans (both labels), where fluopyram was not the residue present at the highest level, the TRR levels of the predominant metabolites were relatively low. In pepper, TRRs of the predominant residues were 0.01-0.026 ppm; in potato tuber, 0.003-0.006 ppm and in beans, 0.008-0.077 ppm.

The metabolism in all plants was very similar. The main reactions involved were:
hydroxylation of fluopyram to AE C656948-7-hydroxy and AE C656948-8-hydroxy,
conjugation of hydroxylated fluopyram mainly with sugars,
cleavage of the molecule leading to AE C656948-benzamide, AE C656948-pyridyl-acetic acid (PAA) and AE C656948-carboxylic acid (PCA).

The main metabolic reactions were also observed in rats. It was concluded that the plant metabolites AE C656948-7- and 8-hydroxy, AE C656948-benzamide and PAA are toxicologically covered by the data of the rat studies. Tox data for label-specific metabolite PCA were provided and showed that the metabolite is of no toxicological concern.

The metabolism of fluopyram in plants is adequately documented. The residue definition for enforcement purposes in plant commodities is fluopyram. The residue definition for risk assessment purposes is fluopyram + fluopyram-benzamide in oilseeds and legumes, and fluopyram in all other crops.

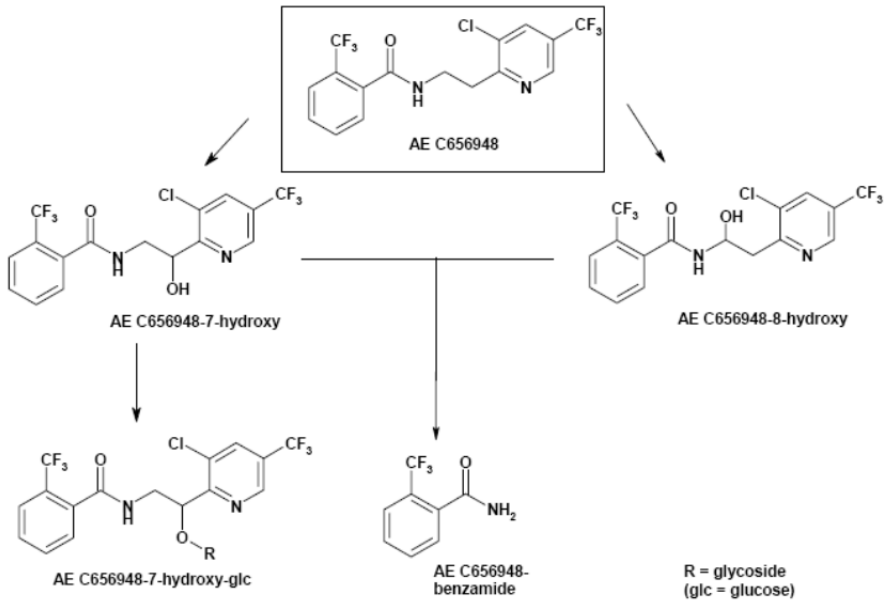


Figure 1. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in grapes.

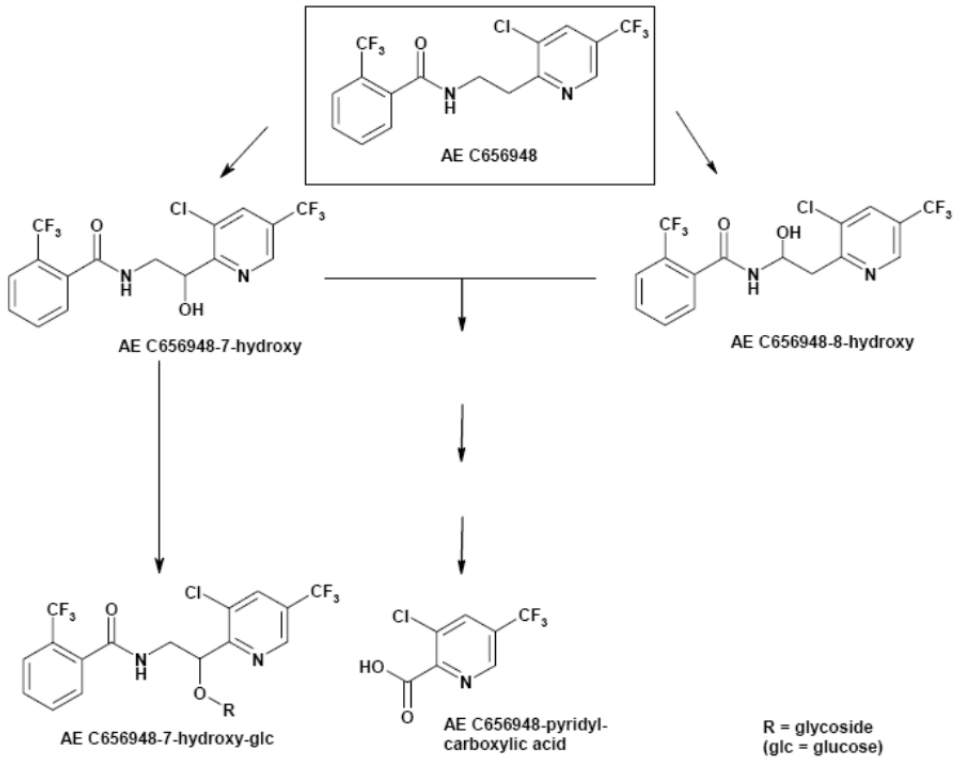


Figure 2. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in grapes.

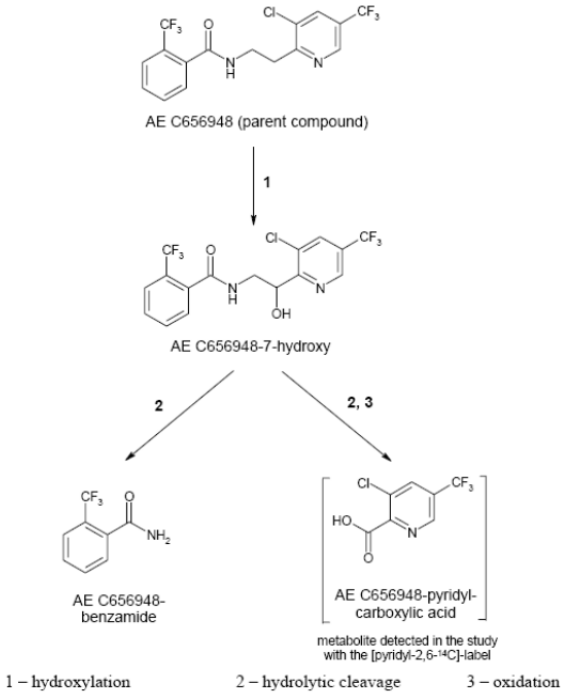


Figure 3. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in potatoes.

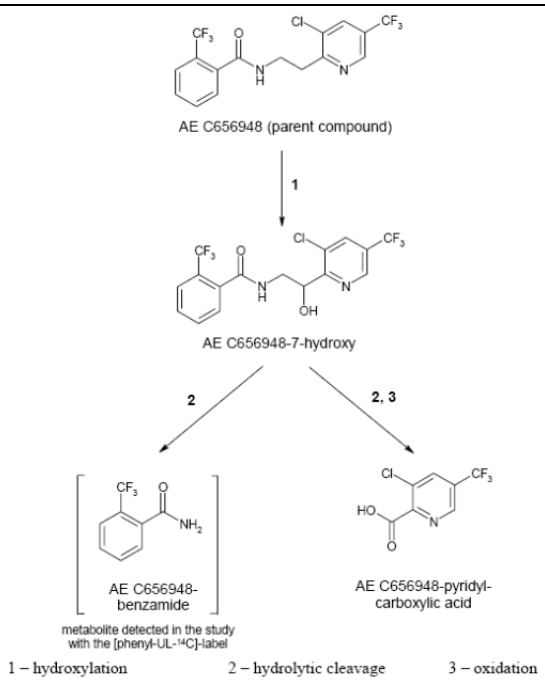


Figure 4. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in potatoes.

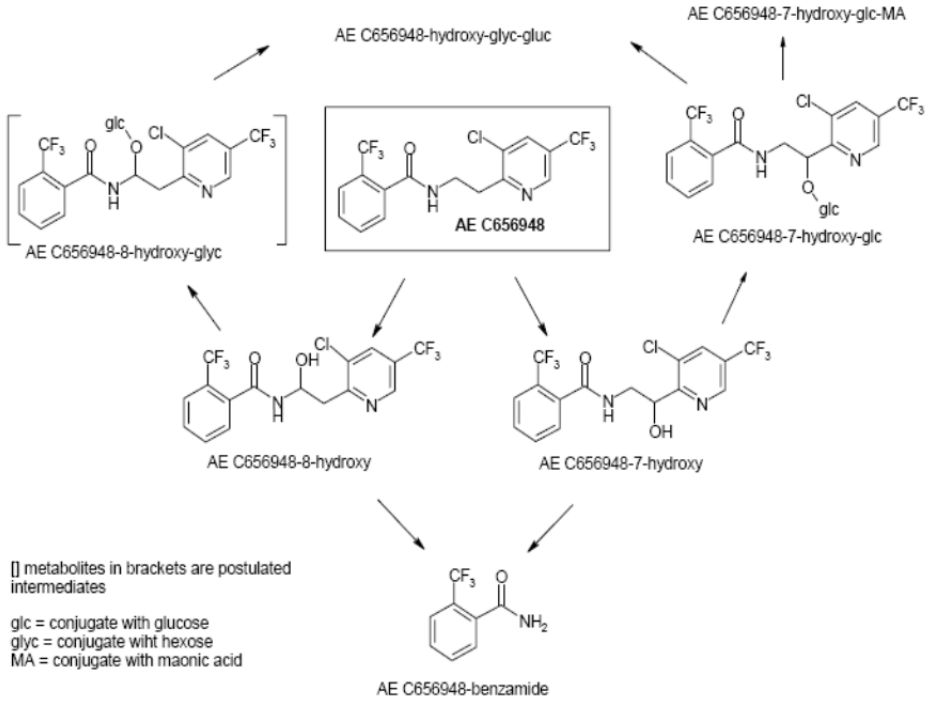


Figure 5. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in beans.

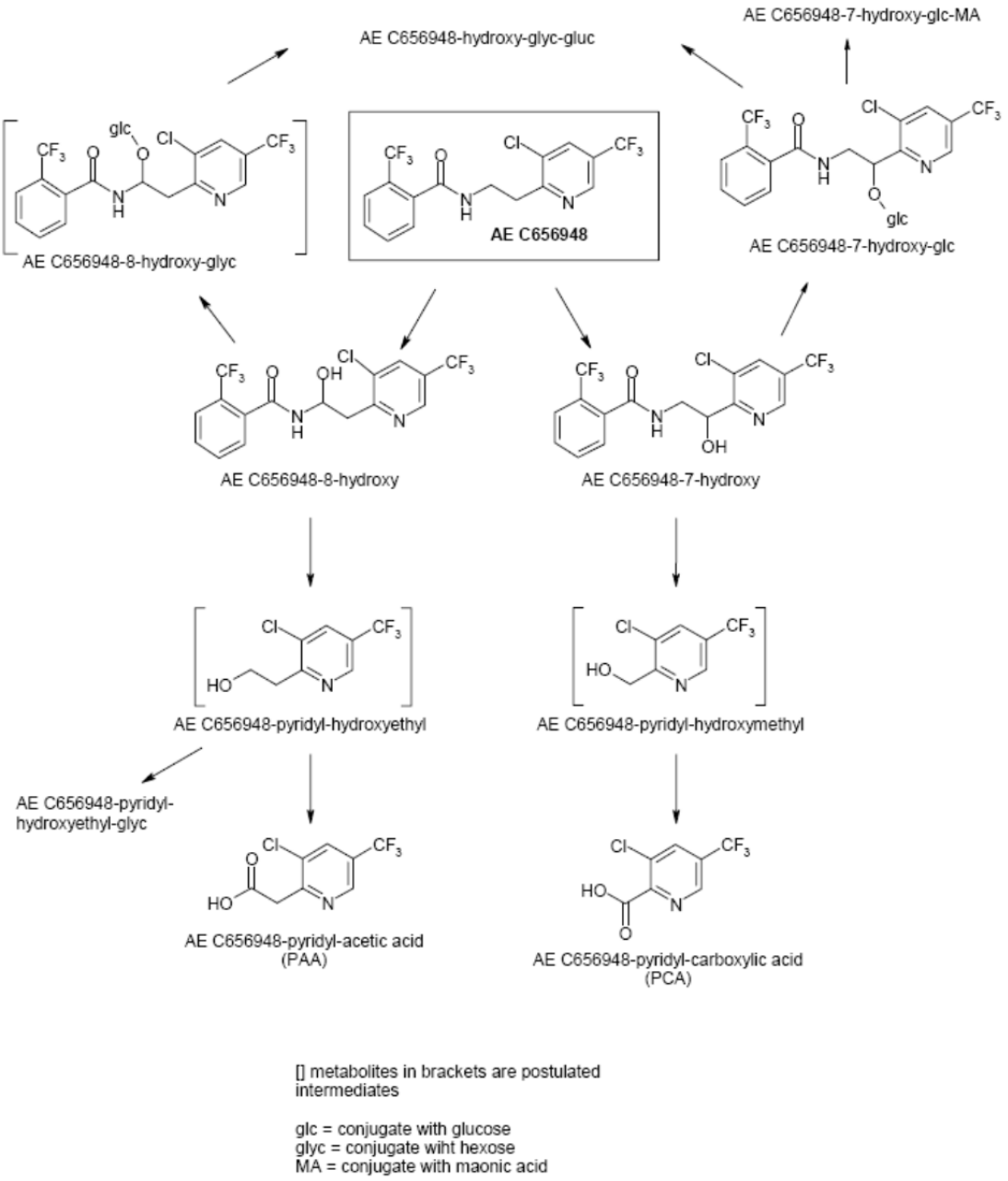


Figure 6. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in beans.

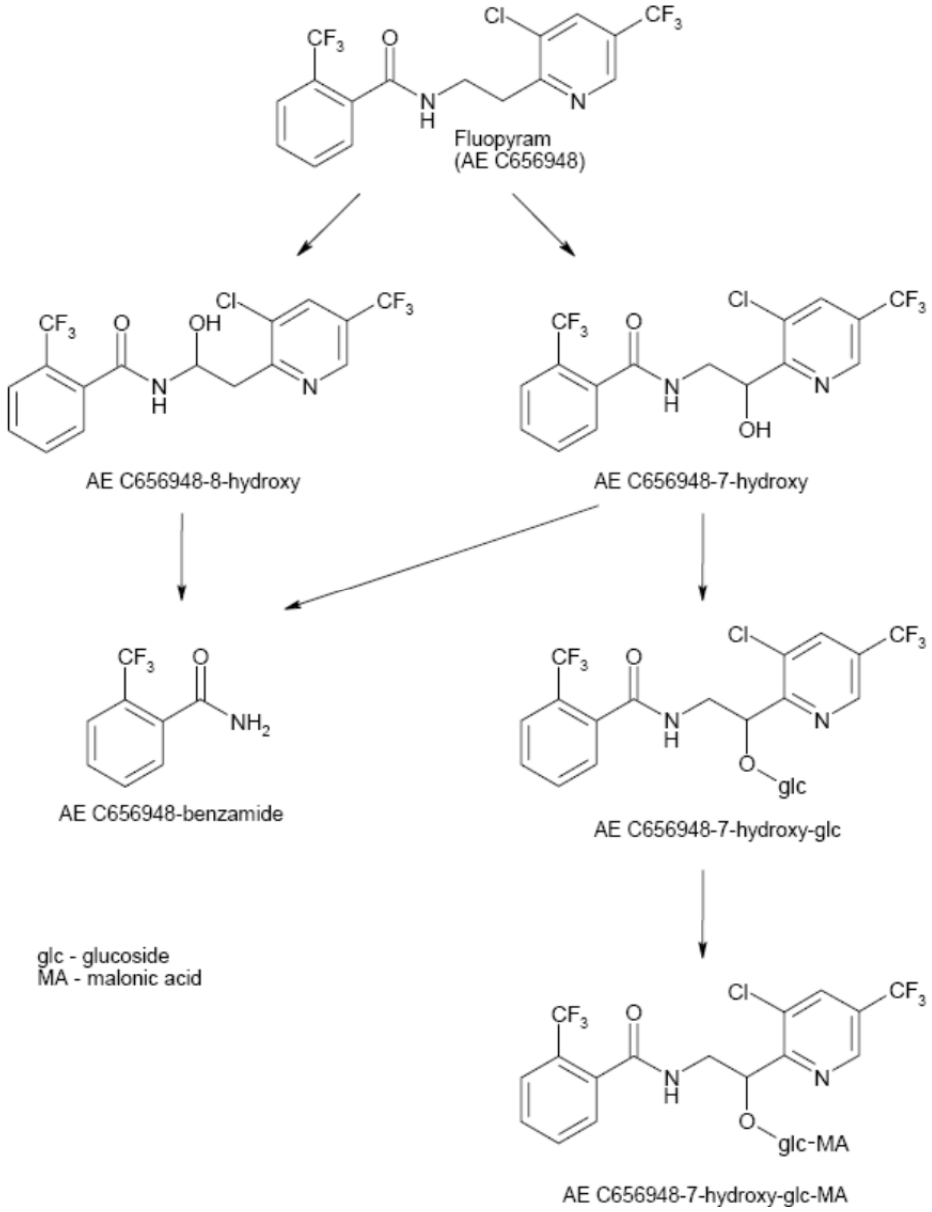


Figure 7. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in red bell peppers.

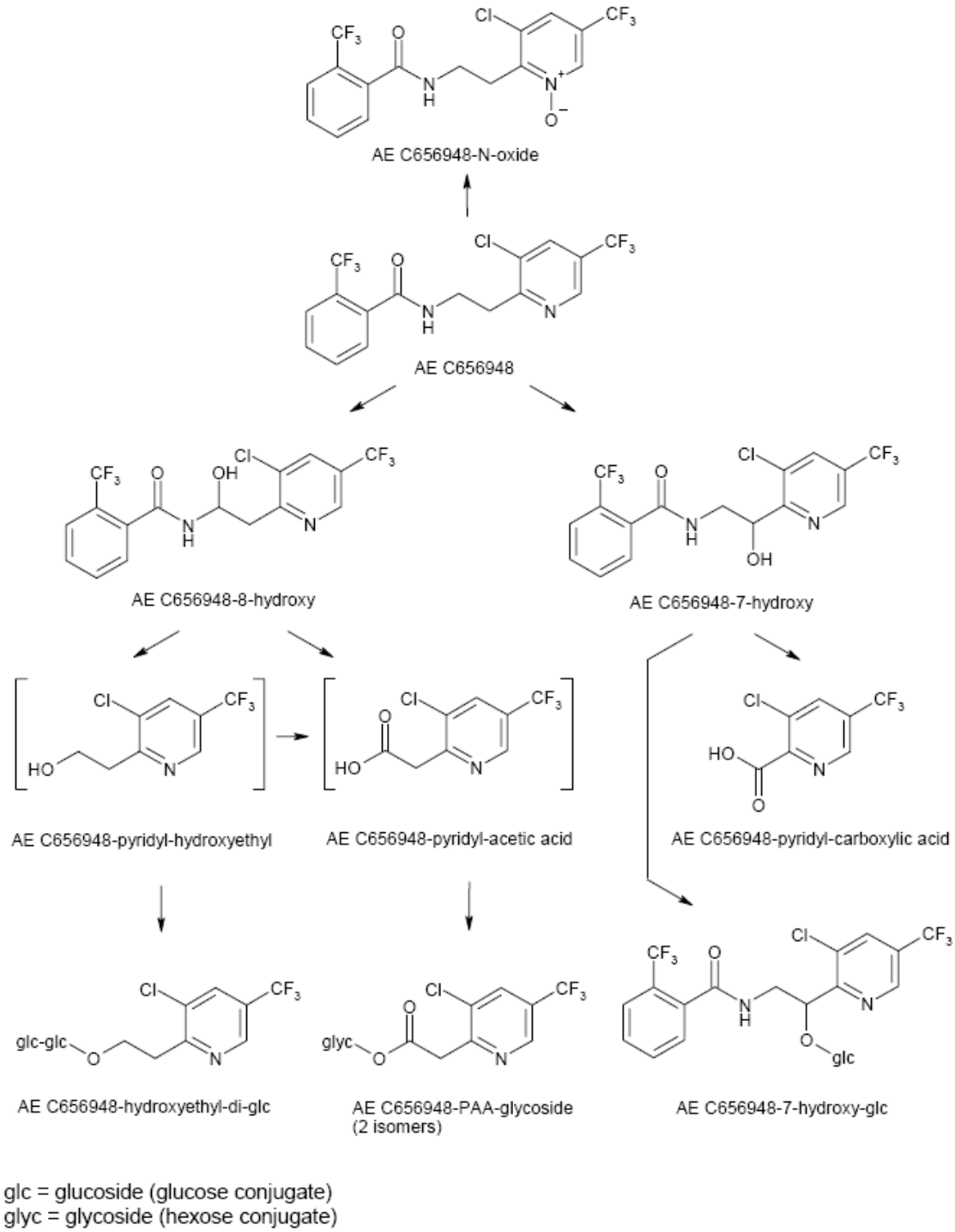


Figure 8. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in red bell peppers.

Table 18b Nature of the Residues in Plant Matrices: Confined Accumulation in Rotational Crops

Confined Accumulation in Rotational Crops – Wheat, Swiss chard, turnip			**PMRA# 1599780 and 1599788**
Radiolabel Position		[phenyl-UL-14C] fluopyram and [pyridyl-2,6-14C] fluopyram	
Test site		Plants were grown in vegetation halls (until cultivation of the 1st rotation) and in greenhouses (2nd and 3rd rotations)	
Formulation used		Soluble concentrate (SC) formulation [AE C656948 formulated as SC500]	
Application rate and timing		Soil was treated at 534 g a.i./ha (phenyl) or 514-g a.i./ha (pyridyl) and aged for 30, 139 and 280 days	
Metabolites Identified			
Matrix	**PBI (days)**	**Major Metabolites (>10% TRR)**	**Minor Metabolites (<10% TRR)**
Phenyl-UL-C14			
Wheat forage	30	Fluopyram	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
Wheat hay	30	Fluopyram	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram AE C656948-7-hydroxy	AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-8-hydroxy

Wheat straw	30	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram AE C656948-7-hydroxy	AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
Wheat grain	30	Fluopyram	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1) AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram AE C656948-benzoic acid	AE C656948-benzamide AE C656948-7-hydroxy
	280	Fluopyram AE C656948-benzoic acid	AE C656948-benzamide AE C656948-7-hydroxy
Swiss chard	30	Fluopyram AE C656948-benzamide AE C656948-7-hydroxy	AE C656948-7-hydroxy-glc-MA (isomer 1) AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
	139	Fluopyram AE C656948-7-OH-SA AE C656948-7-hydroxy	AE C656948-benzamide AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
	280	Fluopyram AE C656948-benzamide AE C656948-7-OH-SA AE C656948-7-hydroxy	AE C656948-7-hydroxy-glc
Turnip tops (leaves)	30	Fluopyram AE C656948-phenol-glc	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram AE C656948-phenol-glc	AE C656948-benzamide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram AE C656948-benzamide AE C656948-phenol-glc	AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-hydroxy AE C656948-8-hydroxy

Turnip roots	30	Fluopyram	AE C656948-benzoic acid AE C656948-benzamide AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-benzamide AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Not extracted due to low residues (<0.01 mg/kg)	
Pyridyl-2,6-C14			
Wheat forage	30	Fluopyram AE C656948-pyridyl carboxylic acid	AE C656948-7-hydroxy-glc-MA (isomer 1) AE C656948-7-hydroxy-glc AE C656948-7-hydroxy
	139	Fluopyram	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy
Wheat hay	30	Fluopyram	AE C656948- pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy
Wheat straw	30	Fluopyram	AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-methyl-sulfoxide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy

	280	Fluopyram AE C656948-7-hydroxy	AE C656948-methyl-sulfoxide AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-8-hydroxy-glc-MA AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
Wheat grain	30	Fluopyram AE C656948- pyridyl carboxylic acid	AE C656948-methyl-sulfoxide AE C656948-7-hydroxy
	139	Fluopyram AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid	AE C656948-7-hydroxy
	280	Fluopyram AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid	AE C656948-7-hydroxy
Swiss chard	30	Fluopyram AE C656948-7-hydroxy	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
	139	Fluopyram AE C656948-7-OH-SA AE C656948-7-hydroxy	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
	280	Fluopyram AE C656948-7-OH-SA AE C656948-7-hydroxy	AE C656948-methyl-sulfoxide AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc AE C656948-8-hydroxy
Turnip tops (leaves)	30	Fluopyram AE C656948-phenol-glc	AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram AE C656948-phenol-glc	AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
	280	Fluopyram AE C656948-phenol-glc	AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy-glc-MA (isomer 1&2) AE C656948-7-OH-SA AE C656948-7-hydroxy-glc AE C656948-7-hydroxy AE C656948-8-hydroxy
Turnip roots	30	Fluopyram	AE C656948-pyridyl carboxylic acid AE C656948-7-hydroxy AE C656948-8-hydroxy
	139	Fluopyram	AE C656948-7-hydroxy
	280	Fluopyram	AE C656948-7-hydroxy

Proposed Metabolism in Rotational Crops

Confined rotational crop studies conducted at ~500 g a.i./ha on three diverse crops (wheat, Swiss chard and turnips) showed similar metabolic profiles as the ones observed in primary crops (pepper, grapes, beans and potato), with fluopyram being a major compound in all crops over all plant-back intervals. The TRRs for wheat grain, Swiss chard and turnip roots were 0.57 ppm or less and declined with the increase of PBIs. Except for fluopyram, the highest single compound measured in wheat grain, Swiss chard and turnip roots amounted to 0.23 ppm or less.

Based on the results of the confined rotational crops studies, the following predominant metabolites were observed:
Wheat grain: Fluopyram, fluopyram-PCA and fluopyram-methyl sulfoxide
Swiss chard: Fluopyram, fluopyram-7-hydroxy, fluopyram-7-OH-SA (sulphate conjugate) and fluopyram-benzamide
Turnip root: Fluopyram

The residue definition for enforcement purposes is fluopyram in rotational crops.

The residue definition for risk assessment purposes is fluopyram + fluopyram-benzamide in rotational oilseeds and legumes, and fluopyram in all other rotational crops.

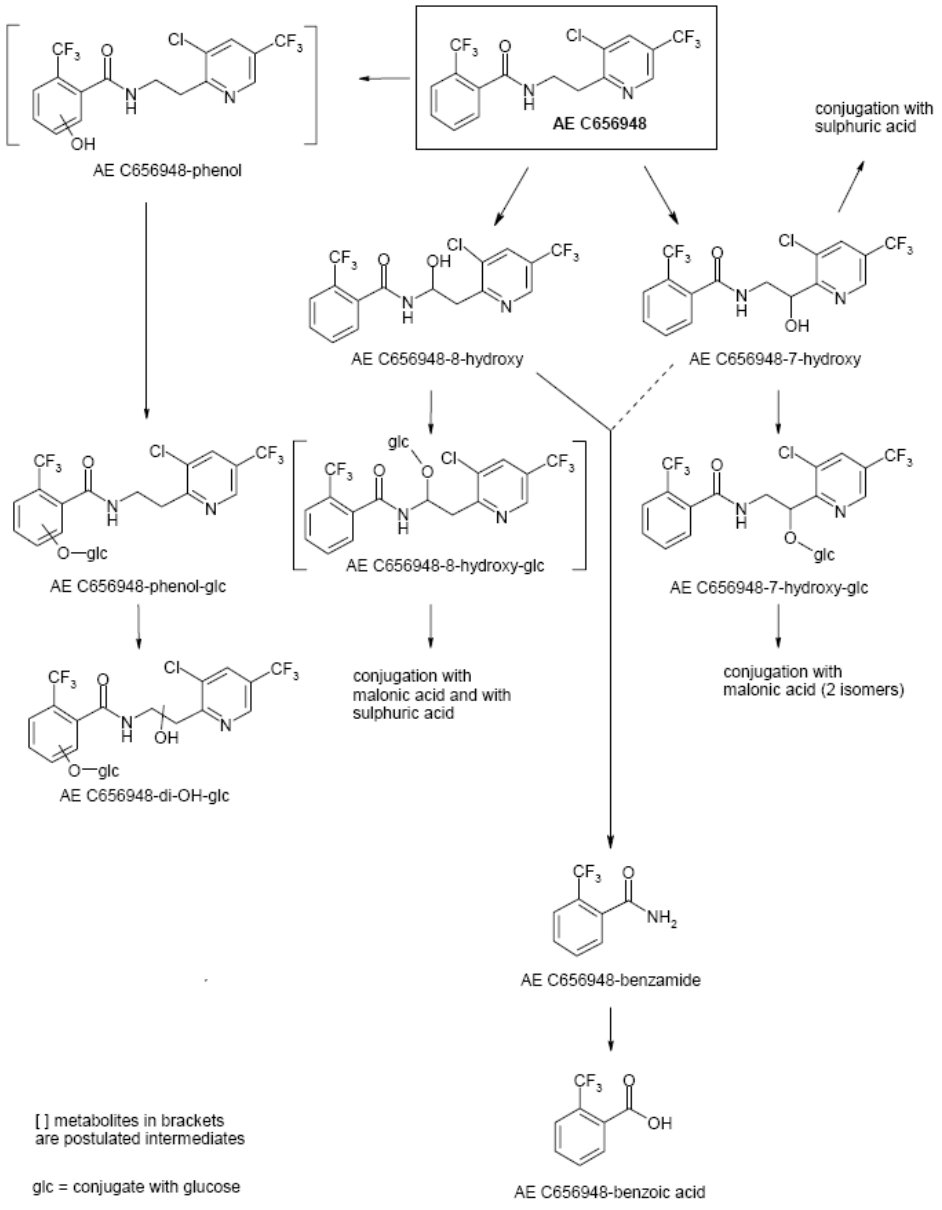


Figure 9. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in rotational crops.

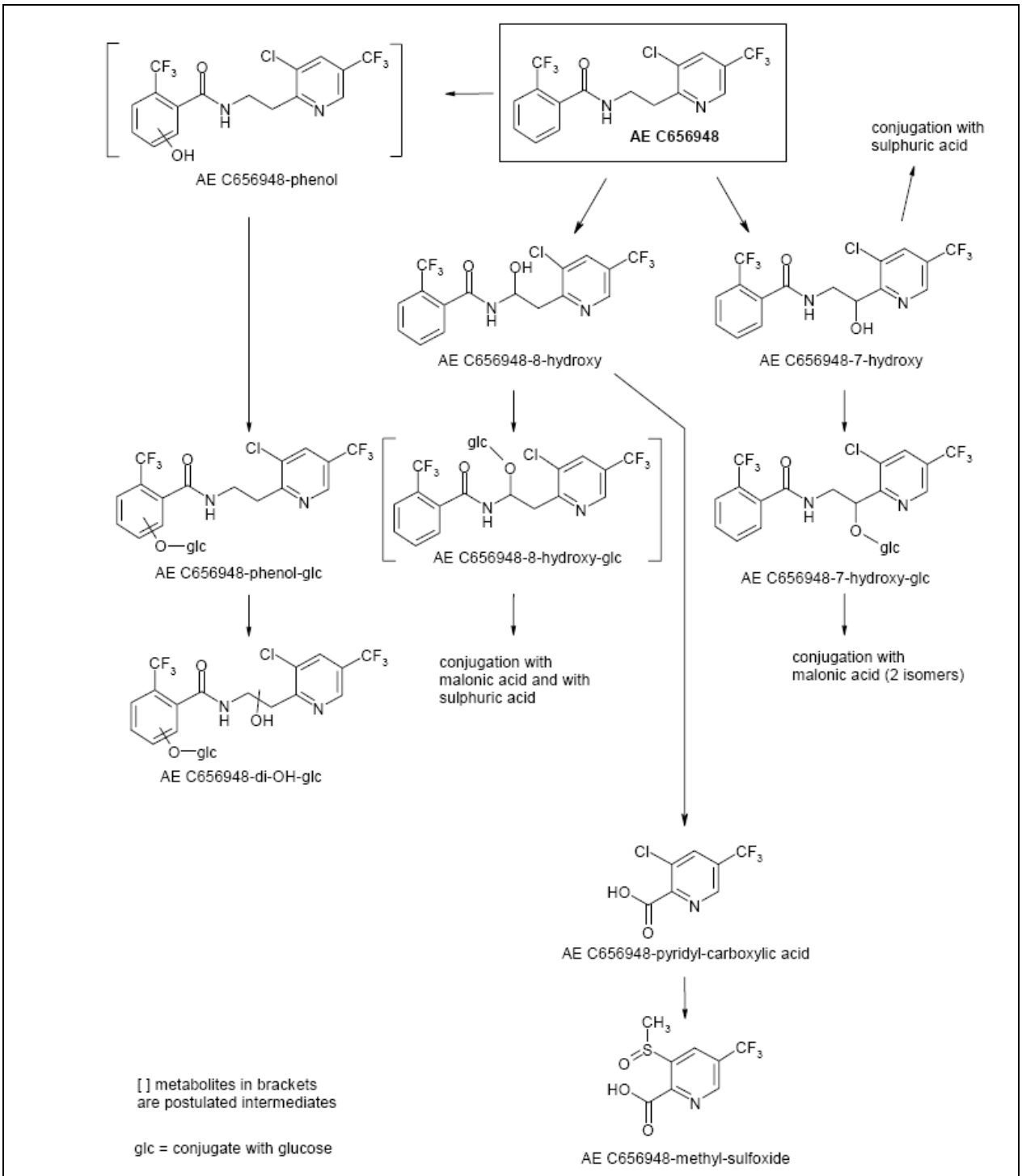


Figure 10. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in rotational crops.

Table 18c Nature of the Residues in Livestock

Nature of the Residue in Laying Hen	**PMRA # 1599784 and 1599792**

Six laying hens (White Leghorn) were administered a single daily oral dose (in the morning by gavage using a syringe) for 14 consecutive days with either 2.03 mg per kg body weight per day (corresponding to 26.42 mg a.i./kg feed/day) for [phenyl-UL-^{14}C]fluopyram or 2.02 mg per kg body weight per day (corresponding to 25.96 mg a.i./kg feed/day) for [pyridyl-2,6-^{14}C]fluopyram. Animals were sacrificed about 24h after the last dose.

Phenyl Radiolabel: The overall recovery (sum of radioactivity in the excreta, eggs as well as tissues) was 94.83% of the total administered dose. The majority of the radioactivity (82.67% of the total dose) was detected in the excreta collected before sacrifice. An amount of 4.34% of the total dose was detected in the eggs. At sacrifice the compound-related residues in the edible organs and tissues amounted to 7.83% of the total dose.

The most important metabolic reaction in the laying hen was the cleavage of the aliphatic chain, yielding the major metabolite AE C656948-benzamide. A second major metabolic reaction involved the hydroxylation of the aliphatic chain followed by elimination, yielding the olefines. Hydrolysis of the amide to a carboxylic acid group was observed as a minor reaction.

Pyridyl Radiolabel: The overall recovery was 95.55% of the total administered dose. The majority of the radioactivity (94.71% of the total dose) was detected in the excreta collected before sacrifice. An amount of 0.36% of the total dose was detected in the eggs. At sacrifice the compound-related residues in the edible tissues collected from the hens amounted to 0.48% of the total dose.

The metabolic reactions in the laying hen were hydroxylation of the aliphatic chain followed by elimination, as well as oxidative cleavage of the aliphatic chain.

The results are in very good agreement with the results from the laying hen metabolism study with [phenyl-UL-^{14}C] fluopyram. The metabolism of fluopyram in hens is well understood.

Matrices	**% of Administered Dose**			
	[phenyl-^{14}C]		**[pyridyl-^{14}C]**	
	TRRs (ppm) (mean of 6 hens)	**% of Administered Dose**	**TRRs (ppm) (mean of 6 hens)**	**% of Administered Dose**
Excreta (day 1-14)	10.655	82.67	12.642	94.71
Total Body Muscle	3.290	4.94	0.831	0.10
Total Body Fat	1.696	0.76	0.498	0.22
Total Body Skin	2.533	0.38	0.152	0.02
Liver	9.536	0.86	0.538	0.05
Kidney	5.759	0.15	0.242	0.01
Eggs (day 1-14)	2.870	4.34	0.235	0.36
Eggs (day 1-6)	1.811	--	0.156	--
Eggs (day 7-14)	3.581	--	0.286	--
Total	--	94.83	--	95.55
Metabolites identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[phenyl-^{14}C]**	**[pyridyl-^{14}C]**	**[phenyl-^{14}C]**	**[pyridyl-^{14}C]**
Eggs	AE C656948-benzamide	Fluopyram AE C656948-Z-olefine	Fluopyram AE C656948-Z-olefine	AE C656948-E-olefine AE C656948-PAA AE C656948-7-hydroxy
Muscle	AE C656948-benzamide	AE C656948-Z-olefine	AE C656948-Z-olefine	Fluopyram AE C656948-E-olefine
Fat	AE C656948-benzamide AE C656948-Z-olefine	Fluopyram AE C656948-Z/E-olefine	Fluopyram AE C656948-E-olefine	None
Liver	AE C656948-benzamide	AE C656948-E-olefine	AE C656948-Z/E-olefine AE C656948-benzoic acid	AE C656948-Z-olefine AE C656948-PAA AE C656948-7-hydroxy

Nature of the Residue in Lactating Goat	**PMRA # 1599783 and 1599791**

One lactating goat (Bunte deutsche Edelziege) was administered a single daily dose via a gelatine capsule on five consecutive days with either 1.91 mg [phenyl-UL-^{14}C] fluopyram per kg body weight per day (corresponding to 46.26 mg a.i./kg feed/day) or with 2.0 mg [pyridyl-2,6-^{14}C] fluopyram per kg body weight per day (corresponding to 44.62 mg a.i./kg feed/day). The animals were sacrificed at about 24h after the last dose.

Phenyl Radiolabel: The overall recovery (sum of radioactivity in the excreta, milk as well as organs and tissues) was 93.46% of the total administered dose. The high urinary excretion during the whole testing period and the findings in the tissues suggest that a considerable amount from each oral dose was bioavailable. Up to the time of sacrifice, the excretion accounted for about 88.31% of the total dose. A high portion of 52.62% was found in the urine and 35.69% in the feces.

The metabolic reactions of [phenyl-UL-^{14}C]fluopyram detected in the lactating goat were:

- hydroxylation of the ethylene bridge of the molecule resulting in AE C656948-7-hydroxy, AE C656948-8-hydroxy, and a dihydroxylated compound,
- hydroxylation of the phenyl ring leading to AE C656948-phenol,
- conjugation of the hydroxylated metabolites with glucuronic acid,
- elimination of water from compounds hydroxylated in the ethylene bridge leading to AE C656948-Z-olefine and E-olefine, E- and Z-olefine can isomerise into each other,
- cleavage of the aliphatic chain to form AE C656948-benzamide,
- hydroxylation of AE C656948-benzamide followed by conjugation with sulphate.

Pyridyl Radiolabel: The overall recovery was 81.89% of the total administered dose. Up to the time of sacrifice, the excretion accounted for 80.95% of the total dose. A high portion of 52.33% was found in the urine and 28.62% in the feces.

The metabolic reactions of [pyridyl-2,6-^{14}C]fluopyram detected in the lactating goat were:

- hydroxylation of the ethylene bridge of the molecule resulting in AE C656948-7-hydroxy, AE C656948-8-hydroxy, and a dihydroxylated compound,
- hydroxylation of the phenyl ring leading to AE C656948-phenol,
- conjugation of the hydroxylated metabolites with glucuronic acid,
- elimination of water from compounds hydroxylated in the ethylene bridge leading to AE C656948-Z-olefine and E-olefine (E- and Z-olefine can isomerize into each other),
- molecular cleavage to AE C656948-pyridyl-hydroxyethyl followed by conjugation with glucuronic acid,
- oxidation of AE C656948-pyridyl-hydroxyethyl to AE C656948-pyridyl-acetic acid.

The results are in very good agreement with the results from the lactating goat metabolism study with [phenyl-UL-^{14}C] fluopyram. The metabolism of fluopyram in goats is well understood.

Matrices	**% of Administered Dose (AD)**			
	[phenyl-^{14}C]		**[pyridyl-^{14}C]**	
	TRRs (ppm)	**% of AD**	**TRRs (ppm)**	**% of AD**
Urine (0-120 h)	29.717	52.62	13.682	52.33
Feces (0-120 h)	7.258	35.69	5.444	28.62
Total Body Muscle	0.737	2.31	0.042	0.12
Total Body Fat	0.399	0.50	0.372	0.42
Kidney	2.295	0.07	0.403	0.01
Liver	8.379	1.71	1.427	0.31
Milk (0-120 h)	0.259	0.56	0.032	0.08
Morning milk	0.276	--	--	--
Evening Milk	0.228	--	0.053	--
Total	--	93.46	--	81.89

Metabolites identified	Major Metabolites (>10% of the TRRs)		Minor Metabolites (<10% of the TRRs)	
Radiolabel Position	**[phenyl-^{14}C]**	**[pyridyl-^{14}C]**	**[phenyl-^{14}C]**	**[pyridyl-^{14}C]**
Milk	AE C656948-benzamide	Fluopyram AE C656948-Z-olefine AE C656948-7-hydroxy	Fluopyram AE C656948-Z-olefine AE C656948-7-hydroxy AE C656948-7-OH-GA AE C656948-benzamide-SA	AE C656948-7-OH-GA AE C656948-8-OH-GA AE C656948-E-olefine
Muscle	AE C656948-benzamide	Fluopyram AE C656948-Z-olefine AE C656948-7-hydroxy	AE C656948-7-hydroxy AE C656948-7-OH-GA AE C656948-benzamide-SA	AE C656948-7-OH-GA AE C656948-8-OH-GA AE C656948-E-olefine
Fat	Fluopyram AE C656948-benzamide AE C656948-Z-olefine	Fluopyram AE C656948-Z-olefine AE C656948-7-hydroxy	AE C656948-E-olefine AE C656948-7-hydroxy	AE C656948-E-olefine
Liver	AE C656948-benzamide	AE C656948-7-OH-GA	Fluopyram AE C656948-Z/E-olefine AE C656948-7-hydroxy AE C656948-7-OH-GA AE C656948-8-OH-GA AE C656948-benzamide-SA AE C656948-phenol-GA	Fluopyram AE C656948-phenol-GA AE C656948-di-OH-GA AE C656948-8-OH-GA AE C656948-E-olefine AE C656948-7-hydroxy
Kidney	AE C656948-benzamide	AE C656948-7-OH-GA	Fluopyram AE C656948-7-hydroxy AE C656948-7-OH-GA AE C656948-8-OH-GA AE C656948-benzamide-SA AE C656948-phenol-GA AE C656948-di-OH-GA	AE C656948-PAA AE C656948-hydroxyethyl-GA AE C656948-phenol-GA AE C656948-di-OH-GA AE C656948-8-OH-GA AE C656948-E-olefine AE C656948-7-hydroxy

Proposed Metabolism in Livestock

The metabolism of fluopyram in goat and hen is very similar. The main reactions involved are:

- hydroxylation of fluopyram to AE C656948-7-hydroxy and AE C656948-8-hydroxy,
- elimination of water from compounds hydroxylated in the ethylene bridge leading to AE C656948-Z/E-olefines,
- cleavage of the molecule leading to AE C656948-benzamide and AE C656948-pyridyl-acetic acid (PAA),
- conjugation of the hydroxylated fluopyram mainly with glucuronic acid.

The metabolic pathways were similar to the ones in rat, except for the 2 isomers of fluopyram-(Z/E)-olefine which were predominant metabolites in both hen and goat matrices [not seen in rat metabolism studies; seen minimally (≤0.007 ppm) in the rat organ depletion study, in liver, kidney and perirenal fat]. It was concluded that metabolites AE C656948-benzamide and PAA are toxicologically covered by the data of the rat studies. Based on similar structure to fluopyram (and fluopicolide which is less toxic than fluopyram), fluopyram-(Z/E)-olefines are considered to be not more toxic.

The metabolism of fluopyram in animals is adequately documented. **The residue definition for enforcement purposes in animal commodities is fluopyram including the metabolite fluopyram-benzamide (expressed as parent equivalent). The residue definitions for risk assessment purposes are:**

- In poultry tissues and eggs: Fluopyram including the metabolites fluopyram-benzamide and fluopyram-olefines (total of 2 isomers) (expressed as parent equivalent)
- In ruminant tissues and milk: Fluopyram including the metabolites fluopyram-benzamide, fluopyram-olefines (total of 2 isomers) and fluopyram-7-hydroxy (expressed as parent equivalent). {Fluopyram-7-hydroxy was not analyzed in the feeding studies; it can be considered by a ratio (conversion factor) derived from the goat metabolism study with fluopyram as reference to determine the input value for risk assessment.}

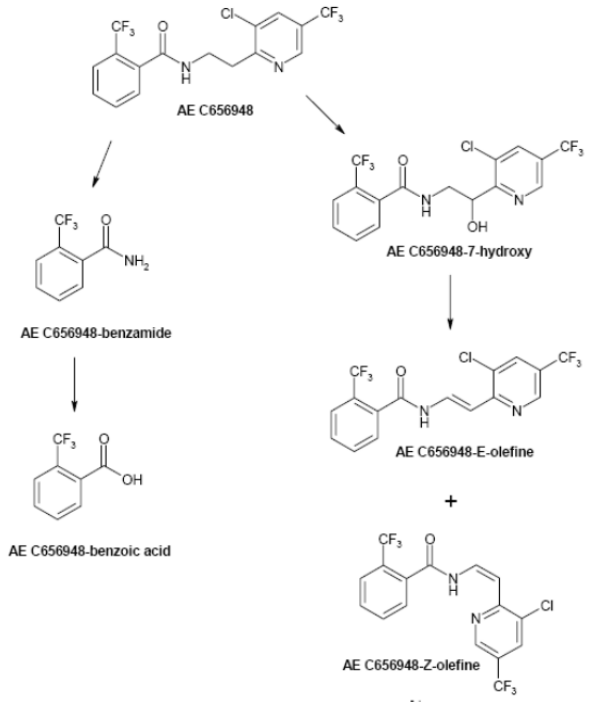


Figure 11. Proposed metabolic pathways of [phenyl-UL-^{14}C] fluopyram in laying hen.

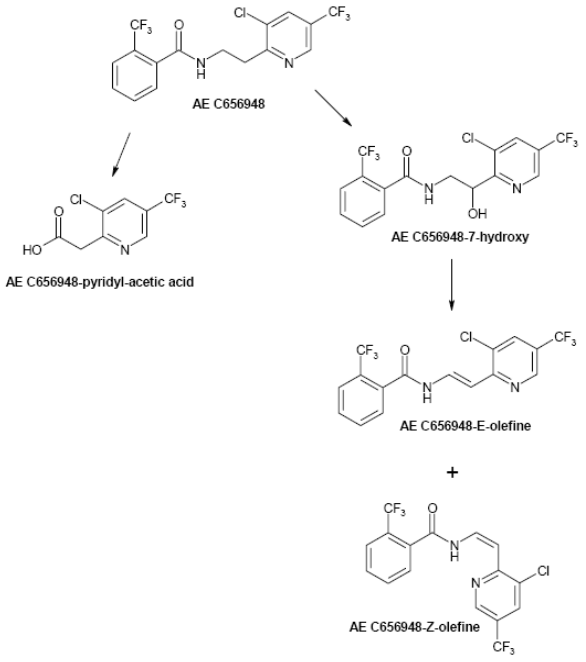


Figure 12. Proposed metabolic pathways of [pyridyl-2,6-^{14}C] fluopyram in laying hen.

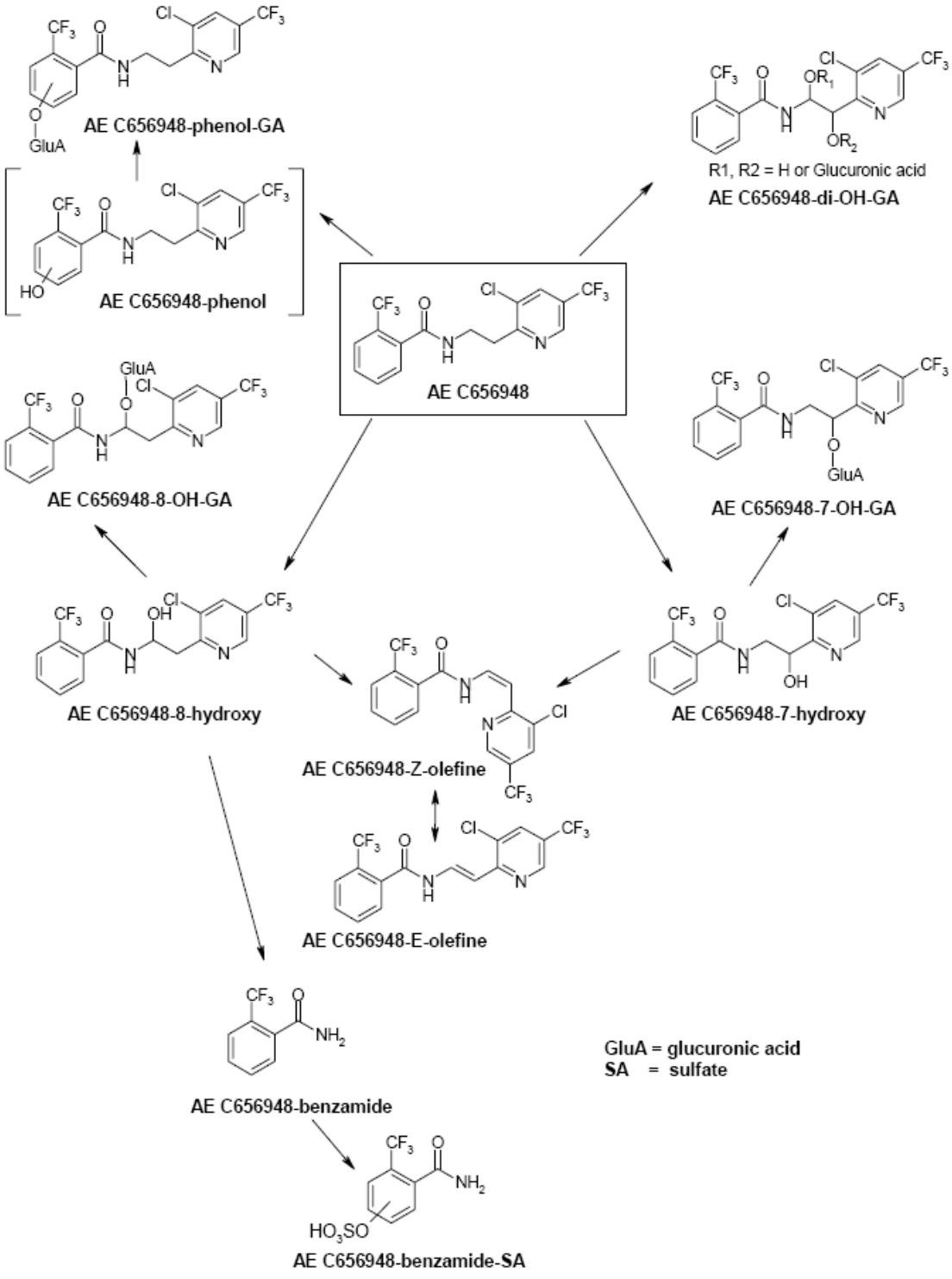


Figure 13. Proposed metabolic pathways of [phenyl-UL-^{14}C] fluopyram in lactating goat.

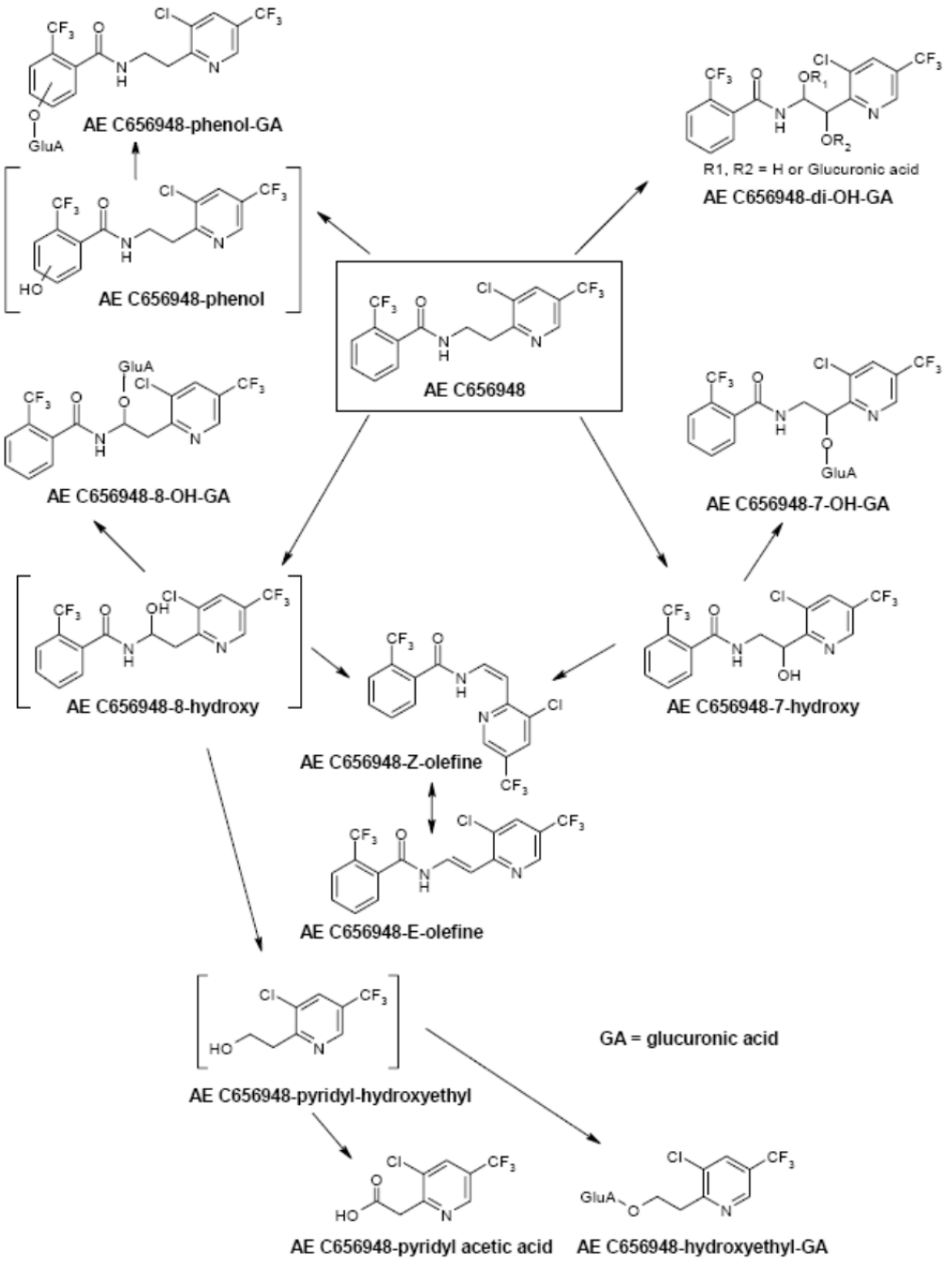


Figure 14. Proposed metabolic pathways of [pyridyl-2,6-^{14}C] fluopyram in lactating goat.

Table 18d Freezer Storage Stability

Freezer Storage Stability	PMRA# 1599821, 1784472, 1983731, 1599801, 1804905, 1983732
Residues of fluopyram and the metabolite fluopyram-benzamide are stable for up to 36 months at ≤-18°C in lettuce head, wheat grain, rape seed, dry pea seed and orange. Stability of Other Metabolites: Fluopyram-pyridyl-acetic acid: up to 36 months in/on lettuce head, wheat grain, rape seed and dry pea seed. Fluopyram-pyridyl-carboxylic acid: up to 36 months in dry pea seed, rape seed and orange. Fluopyram-7-hydroxy: up to 36 months in/on wheat grain and lettuce.	

Table 18e Crop Field Trials and Residue Decline

Crop Field Trials & Residue Decline – Potatoes — **PMRA# 1654363**

Sixteen residue trials (14 harvest and 2 decline) were conducted in 2006 (in NAFTA Growing Regions 1, 2, 3, 5, 9 and 11) on potatoes, the representative crop of Crop Group 1C. At each test location, potatoes were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha/application with a 3- to 5-day application interval for a total seasonal rate of 500 g a.i./ha. The applications were made at BBCH growth stage 45 to 93 (BBCH 45: 50% of total final tuber mass reached; BBCH 93: most of leaves yellowish). Mature potato tubers were harvested at a PHI of 6-7 days. All applications were made using ground-based equipment.

At the PHI of 6-7 days, residues of fluopyram ranged from <0.01 ppm to 0.017 ppm in potato tubers (quantifiable residues were observed in only one out of the 16 trials). Fluopyram residues from both decline trials were less than the LOQ (<0.01ppm) at all time points (PHIs of 0, 3, 7, 14 and 21 days) except for the last time point of one decline trial where residues were slightly above the LOQ.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Potato tubers	500	6-7	32	<0.01	0.017	0.016	<0.01	<0.01	0.004

Crop Field Trials & Residue Decline – Sugar beets — **PMRA# 1654364**

Twelve residue trials (11 harvest and 1 decline) were conducted in 2006 (in NAFTA Growing Regions 5, 7, 8, 9, 10 and 11) on sugar beets. At each test location, sugar beets were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha/application with a 7-day application interval for a total seasonal rate of 500 g a.i./ha. The first application was made at BBCH growth stage 49 (BBCH 49: expansion complete, typical form and size of roots reached). Mature crops were harvested at a PHI of 5-7 days. All applications were made using ground-based equipment.

At the PHI of 6-7 days, residues of fluopyram ranged from 0.01 to 0.05 ppm in sugar beet roots, and from 0.27 to 18.7 ppm in sugar beet tops. In the residue decline trial, samples were harvested at PHIs of 0, 6, 13, 19 and 27 days. Mean residue level dropped from 0.07 ppm to 0.01 ppm in sugar beet roots and from 9.50 ppm to 0.04 ppm in sugar beet tops between PHIs of 0 and 27 days.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Sugar beet roots	500	6-7	24	0.013	0.050	0.040	0.026	0.029	0.011
Sugar beet tops			24	0.273	18.703	16.510	0.803	3.299	4.888

Crop Field Trials & Residue Decline – Dry beans and peas **PMRA# 1661215**

Nine residue trials (8 harvest and 1 decline) were conducted in 2006 (in NAFTA Growing Regions 5, 7, 8, 9, 10 and 11) on dry beans. At each test location, dry beans and peas were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application for a total seasonal rate of 500 g a.i./ha. All applications were made using ground-based equipment.

Each trial had two treated plots (TRTD1 and TRTD2). In plot TRTD1 of the dry bean trials, the 1st application was made at a BBCH growth stage between 28 (eight side shoots detectable) and 59 (first petals visible, still closed). The 2nd application to TRTD1 was made 5-8 days later, and forage was harvested at a 0-day PHI at a target growth stage between BBCH 30 and 59. In plot TRTD2 of the dry bean trials, the 1st application was made at a BBCH growth stage between 67 (flowering declining) and 86 (60% of pods ripe and dark, seeds dry and hard). The 2nd application to TRTD2 was made 5-7 days later, and hay was harvested at a 0-day PHI at a target growth stage between BBCH 85 to 89. Seed was also harvested (plants cut from the ground) from plot TRTD2 at a 13- to 14-day PHI (except one trial with a 0-day PHI) at a target BBCH 89 growth stage. Hay and seed were allowed to dry to commercial dryness prior to sampling.

At the PHI of 13-14 days, residues of fluopyram ranged from <0.01 to 0.08 ppm in dry beans and 0.03 to 0.35 ppm in dry peas. In the residue decline trials, seed samples were harvested at PHIs of 0, 7, 14, 17-18 and 22-24 days. Mean residue level dropped from 0.052 ppm to 0.017 ppm in dry beans between PHIs of 0 and 22 days. Residues remained approximately the same in dry peas at 0.036 ppm and 0.026 ppm between PHIs of 0 and 24 days.

The maximum fluopyram residues in dry bean forage at 0-day PHI were 25.4 ppm. The maximum fluopyram residues in dry pea vines at 0-day PHI were 11.1 ppm. The maximum fluopyram residues in dry bean hay harvested at 0-day PHI were 37.7 ppm. The maximum fluopyram residues in dry pea hay harvested at 0-day PHI were 49.4 ppm.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Dry beans	500	13-14	18	<0.01	0.076	0.068	0.012	0.023	0.022
Dry peas			10	0.03	0.350	0.35	0.058	0.130	0.13

Crop Field Trials & Residue Decline – Melons **PMRA# 1661219**

Six residue trials (5 harvest and 1 decline) were conducted in 2007 (in NAFTA Growing Regions 2, 5, 6 and 10) on muskmelon. At each test location, melons were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with a 5- to 6-day application interval for a total seasonal rate of 500 g a.i./ha. The 1st application to melons was made at BBCH growth stage between 71 (first fruit on main stem has reached typical size and form) and 89 (fully ripe). Mature crops were harvested at a PHI of 0 day. All applications were made using ground-based equipment.

At the PHI of 0 day, residues of fluopyram ranged from 0.07 to 0.53 ppm in muskmelons. In the residue decline trials, samples were harvested at PHIs of 0, 1, 3, 7 and 10 days. Residues remained approximately the same through the 10 days in muskmelons at 0.076 ppm to 0.107 ppm. The practice of peeling muskmelon fruit treated by broadcast foliar spray reduced the total fluopyram residues in muskmelon, giving a processing factor of 0.04X.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Muskmelon	500	0	12	0.069	0.529	0.439	0.192	0.217	0.156

Crop Field Trials & Residue Decline – Apples **PMRA# 1670088**

Seventeen residue trials (14 harvest and 3 decline) were conducted in 2006 and 2007 (in NAFTA Growing Regions 1, 2, 5, 9, 10 and 11) on apples. At each test location, apple trees were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with a 5- to 7-day application interval for a total seasonal rate of 500 g a.i./ha. For all trials, there was one treated plot, which received a low volume (concentrate) spray solution, with spray volumes of 368-671 L/ha. For 12 of the apple trials, there was a second treated plot, which received a high volume (dilute) spray solution, with spray volumes of 1941-2860 L/ha. The first application was made between BBCH growth stage 78 to 89 (BBCH 78: fruit about 80% final size; BBCH 89: fruit ripe for consumption). Mature apples were harvested at a PHI of 7 days. All applications were made using ground-based equipment.

At a PHI of 7 days, residues of fluopyram ranged from 0.04 to 0.25 ppm in apples treated with a concentrated spray and from 0.06 to 0.26 ppm in apples treated with a dilute spray. In the residue decline trials, samples were harvested at PHIs of 0, 3, 7, 10 and 14 days. Mean residue level dropped from 0.16 ppm to 0.08 ppm in apples between PHIs of 0 and 14 days.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Apple	500 (conc. spray)	0	34	0.054	0.796	0.751	0.192	0.225	0.151
		7	34	0.040	0.247	0.242	0.109	0.120	0.063
	500 (dilute spray)	0	24	0.070	0.545	0.437	0.159	0.176	0.092
		7	24	0.057	0.262	0.255	0.086	0.105	0.055
	500	0	4	0.109	0.174	0.167	0.139	0.140	0.031
		7	4	0.061	0.107	0.101	0.083	0.084	0.021

Crop Field Trials & Residue Decline – Cherries **PMRA# 1661231**

Six residue trials (5 harvest and 1 decline) were conducted in 2006 and 2007 (in NAFTA Growing Regions 1, 5, 10 and 11) on cherries. At each test location, cherries were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with a 5- to 8-day application interval for a total seasonal rate of 500 g a.i./ha. Mature crops were harvested at a PHI of 0 day. Spray volumes ranged from 371 to 624 L/ha for plots receiving concentrated sprays and from 1905 to 3350 L/ha for plots receiving diluted sprays. All applications were made using ground-based equipment.

At the PHI of 0 day, residues of fluopyram ranged from 0.07 to 0.64 in cherries treated with the concentrated spray and 0.15 to 1.2 ppm in cherries treated with the dilute spray. In the decline trials, samples were harvested at PHIs of 0, 3, 7, 10 and 14 days. Residues in cherries decreased with time. The normal household practice of washing and cooking cherries significantly reduced fluopyram residues in/on cherries. The processing factors calculated for the washed cherries and the washed and cooked cherries were 0.48X and 0.41X, respectively.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Cherries	500 (conc. spray)	0	12	0.066	0.641	0.639	0.505	0.425	0.223
	500 (dilute spray)	0	12	0.147	1.229	1.174	0.396	0.516	0.349

Crop Field Trials & Residue Decline – Grapes **PMRA# 1599586**

Sixteen residue trials (15 harvest and 1 decline) were conducted in 2006 and 2007 (in NAFTA Growing Regions 1, 5, 10 and 11) on grapes. At each test location, two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha (0.223 lb. a.i./A) were made to grapes at growth stages from fruit ripe for picking to fruit ripe for consumption (BBCH 87 to 89) with a 12 to 14 day application interval for a seasonal rate of 500 g a.i./ha, 3-day and 7-day PHIs on the harvest trials, and 0, 3, 7, 10 and 14 days PHIs for the decline trial.

Residues of fluopyram on grapes ranged from 0.068 ppm to 0.987 ppm at a PHI of 3 days and from 0.096 ppm to 0.950 ppm at a PHI of 7 days. The mean values were 0.458 ppm and 0.401 ppm on day 3 and day 7, respectively. For the decline trial, mean residue level dropped from 0.872 ppm at 0-day PHI to 0.672 ppm at 14-day PHI.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Grapes	439 - 513	6-7	32	0.096	0.950	0.948	0.372	0.401	0.229

Crop Field Trials & Residue Decline – Strawberries **PMRA# 1599587**

Ten residue trials (9 harvest and 1 decline) were conducted in 2007 (in NAFTA Growing Regions 1, 2, 3, 5, 10 and 12) on strawberries.

At each test location for the spray treated plot, two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha were made to strawberry plants at BBCH growth stage 81 to 91 (beginning of ripening to beginning of auxiliary bud formation) with a 5-day application interval for a seasonal rate of 500 g a.i./ha and a 0-day PHI. A second treated plot received two drip irrigation applications of AE C656948 500 SC at a rate of 250 g a.i./ha with a 5-day interval and target PHIs of 0 and 7 days. In the decline trial, duplicate composite samples of strawberries were collected at 0, 3, 7, 10 and 14 days PHI following the final application, for plots treated by foliar spray application and drip line irrigation application.

For the broadcast application trials, fluopyram residues on strawberry fruit at the PHI of 0-day ranged between 0.18 ppm to 1.06 ppm. Data from the decline trial showed that residue levels in/on fruits dropped by about 49% over 14 days. For the drip irrigation application trials, fluopyram residues on strawberry fruit at the PHI of 0 day ranged from <LOQ to 0.11 ppm, and the residues at the PHI of 7 days ranged from <LOQ to 0.24 ppm. In the decline trial, the residue levels on day 0 were <0.01 ppm, and increased to about 0.03 ppm at day 10 and day 14 after last treatment. The residue levels in the drip irrigation trials were 5 to 10 times lower than those observed in the broadcast applications.

Commodity	**Total Appl. Rate (g a.i./ha)**	**PHI (days)**	**Fluopyram Residue Levels (ppm)**						
			n	**Min**	**Max**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Strawberries	495 – 525 (drip irrigation)	0	20	<0.01	0.112	0.10	0.01	0.026	0.028
		7	20	<0.01	0.244	0.23	0.02	0.050	0.069
	491 – 519 (direct broadcast)	0	20	0.183	1.062	1.01	0.395	0.513	0.279
	500 (European greenhouse)	1	8	0.12	0.79	0.79	0.27	0.35	0.26

Crop Field Trials & Residue Decline – Tree Nuts **PMRA# 1661238**

Ten residue trials were conducted in 2006 on tree nuts. Five trials (4 harvest and 1 decline) were conducted on almonds (in NAFTA Growing Region 10) and five trials (4 harvest and 1 decline) were conducted on pecans (in NAFTA Growing Regions 2, 4, 6 and 8). At each test location, nuts were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with a 6- to 7-day application interval in almond and 13- to 14-day interval in pecan for a total seasonal rate of 500 g a.i./ha. Each trial had two treated plots, one for dilute spray applications and one for concentrated spray applications. Samples of mature nuts were harvested at a 14-day PHI. One trial for each of the representative crop was a decline trial where samples were harvested at PHIs of 0, 7, 14, 21 and 28 days. All applications were made using ground-based equipment.

At the PHI of 14 days, residues of fluopyram ranged from <0.01 ppm to 0.019 ppm in almond nutmeat, 1.22 ppm to 6.12 ppm in almond hulls and <0.01 ppm to0.045 ppm in pecan. For the residue decline trials, mean residue level increase from <0.01 ppm on day 0 to 0.018 ppm on day 14 and decrease to 0.013 ppm on day 28 in almond nutmeat. For the residue decline trial in pecans, mean residue level dropped from 0.045 ppm to <0.01 ppm between PHIs of 0 and 14 days and remained <0.01 ppm through 28 days.

Commodity	**Total Appl. Rate (g a.i./ha)**	**PHI (days)**	**Fluopyram Residue Levels (ppm)**						
			n	**Min**	**Max**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Almond Nutmeat	500 (conc. spray)	14	10	<0.01	0.016	0.015	<0.01	<0.01	<0.01
	500 (dilute spray)	14	10	<0.01	0.019	0.018	<0.01	<0.01	<0.01
Almond Hulls	500 (conc. spray)	14	10	1.22	6.12	5.43	2.44	2.97	1.57
	500 (dilute spray)	14	10	1.93	4.45	4.25	3.26	3.18	1.09
Pecans	500 (conc. spray)	14	10	<0.01	0.045	0.031	<0.01	<0.01	0.014
	500 (dilute spray)	14	10	<0.01	0.021	0.018	<0.01	<0.01	<0.01

Crop Field Trials & Residue Decline – Peanuts **PMRA# 1661252**

Twelve residue trials (11 harvest and 1 decline) were conducted in 2007 and 2008 (in NAFTA Growing Regions 2, 3, 6 and 8) on peanuts.

At each test location, peanuts were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with for a total seasonal rate of 500 g a.i./ha. The interval between applications was 12 to 14 days. Applications were timed so that sampling would occur at growth stages from BBCH 89 (fully mature, nearly all pods developed to final size are ripe) to BBCH 97 (above ground parts of plant are dead). In the harvest trials, the representative commodities of peanut nutmeat and peanut hay were harvested at PHIs of 7 (-1) days. In the decline trial, samples of peanuts were collected at PHIs of 0, 3, 7, 10 and 14 days following the application. All applications were made using ground-based equipment.

At the PHI of 7 days, residues of fluopyram ranged from <0.01 ppm to 0.018 ppm in peanut nutmeat and 1.08 to 21.9 ppm in peanut hay. The decline of fluopyram residues with time in peanut nutmeat could not be assessed due to the low levels observed. Fluopyram residues declined with time in peanut hay.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Peanut nutmeat	500	7	24	<0.01	0.018	0.017	<0.01	<0.01	<0.01
Peanut hay		7	24	1.078	21.88	20.66	6.19	8.72	6.78

Crop Field Trials & Residue Decline – Bananas **PMRA# 1661260**

Fourteen residue trials (12 harvest and 2 decline) were conducted in 2007 in Latin America on bananas. At each test location, bananas were treated with six foliar spray applications of AE C656948 500 SC at a rate of 100 g a.i./ha/application with a 5 to 11-day application interval for a total seasonal rate of 600 g a.i./ha. The first application was made at BBCH growth stage between 70 (first fruit visible) and 75 (fruits are 50% of final size). At each trial, single control and duplicate treated samples of bananas (bagged and unbagged) were harvested at commercial maturity, at a PHI of 0 day. In two trials, additional samples were collected at 0, 2-3, 5 and 6-7 day PHIs to monitor residue decline. All applications were made using ground-based equipment.

Residues of fluopyram on bananas (bagged; PHI of 0 day) ranged from <0.01 to 0.04 ppm (mean = 0.018 ppm). Residues of fluopyram on bananas (unbagged; PHI of 0 day) ranged from 0.018 to 0.526 ppm (mean = 0.164 ppm). In the residue decline trials, mean residues in unbagged bananas decreased from 0.04 ppm and 0.17 ppm at the 0-day PHI to <0.01 ppm and 0.13 ppm, respectively, at the 6-7 day PHI.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Bananas (unbagged)	600	0	28	0.018	0.526	0.510	0.144	0.164	0.140

Table 18f Residue Data in Rotational Crops

Residue Data in Rotational Crops – Limited Field Accumulation in Wheat, Turnip and Mustard Greens **PMRA# 1661301**

Three field trials each were conducted in/on rotated wheat, rotated turnips and rotated mustard greens in the US in Zones 3, 4 and 10 during the 2006 growing season.

Rotated wheat: Two foliar spray applications of AE C656948 500 SC were made to cover crops at a rate of 250 to 263 g a.i./ha/application for a total application rate of 505 to 525 g a.i./ha. The actual interval between applications was 5 to 7 days and the actual PBI ranged from 236 to 248 days. The cover crop (wheat) was harvested or destroyed within 0 to 14 days following the final application, in advance of replanting to prepare a suitable seedbed for the rotational crop.

Rotated turnips: Two foliar spray applications of AE C656948 500 SC were made to cover crops at a rate of 245 to 256 g a.i./ha/application for a total application rate of 493 to 511 g a.i./ha. The actual interval between applications was 5 to 7 days and the actual PBI ranged from 228 to 236 days. The cover crop (wheat or soybean) was harvested or destroyed within 0 to 14 days following the final application.

Rotated mustard greens: Two foliar spray applications of AE C656948 500 SC were made to cover crops at a rate of

242 to 254 g a.i./ha/application for a total application rate of 493 to 499 g a.i./ha. The actual interval between applications was 5 to 7 days and the actual PBI ranged from 228 to 236 days. The cover crop (wheat or soybean) was harvested or destroyed within 0 to 14 days following the final application.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat forage	505-525	8	6	<0.01	0.048	0.041	0.010	0.020	0.017
Wheat grain			6	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Wheat hay			6	0.018	0.089	0.082	0.032	0.044	0.030
Wheat straw			6	0.011	0.12	0.12	0.031	0.056	0.054
Turnip roots	493-511	8	6	<0.01	<0.01	<0.01	<0.01	<0.01	NA
Turnip tops			6	<0.01	0.041	0.034	0.018	0.019	0.002
Mustard greens	493-499	8	6	<0.01	0.036	0.035	0.013	0.018	0.014

Residue Data in Rotational Crops - Alfalfa **PMRA# 1654401**

Twelve field trials were conducted in the US during 2007 to measure the magnitude of fluopyram residues in alfalfa planted as a rotational crop. Two foliar spray applications of AE C656948 500 SC were made to bare soil or a cover crop (mustard) at a rate of 240 to 260 g a.i./ha/application for a total application rate of 497 to 514 g a.i./ha. The actual interval between applications was 5 to 6 days and the actual PBI ranged from 12 to 14 days. All applications were made using ground-based equipment. The fields were tilled and fertilized, or the cover crop was shredded, disked under and the soil surface was smoothed, before seeding of alfalfa.

Commodity	Total Appl. Rate (g a.i./ha)	PBI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Alfalfa forage/1	497-514	12-14	24	<0.01	0.39	0.33	0.04	0.07	0.09
Alfalfa forage/2			22	<0.01	0.10	0.10	0.04	0.05	0.03
Alfalfa forage/3			22	0.01	0.19	0.17	0.03	0.05	0.05
Alfalfa hay/1			24	0.02	0.93	0.93	0.09	0.21	0.28
Alfalfa hay/2			22	0.01	0.36	0.35	0.11	0.13	0.11
Alfalfa hay/3			22	0.01	0.46	0.42	0.06	0.13	0.13

Residue Data in Rotational Crops - Cotton **PMRA# 1661299**

Eleven field trials were conducted in the US during 2007 to measure the magnitude of fluopyram residues in cotton planted as a rotational crop. Two foliar spray applications of AE C656948 500 SC were made to bare soil at a rate of 244 to 258 g a.i./ha/application for a total application rate of 495 to 511 g a.i./ha. The actual interval between applications was 1 to 5 days and the actual PBI ranged from 12 to 14 days. All applications were made using ground-based equipment. The fields were tilled, fertilized, and rolled before planting. One trial was cancelled due to crop failure.

Commodity	Total Appl. Rate (g a.i./ha)	PBI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Undelinted cottonseed	495-511	12-14	22	<0.01	<0.01	<0.01	0.01	0.01	NA
Cotton gin byproducts			10	<0.01	0.02	0.02	0.01	0.01	0.01

The following crops were originally requested as primary crops for treatment with fluopyram. It was subsequently requested that cereals, canola and soybeans be considered rotational crops only. The crop field trials were conducted according to the previously proposed Canadian GAP when treated as a primary crop.

Crop Field Trials Used as Rotational Crop Data – Field Corn and Sweet Corn **PMRA# 1661248**

Nineteen residue trials (four sweet corn, ten field corn and five field/sweet corn) were conducted (in NAFTA Growing Regions 1, 2, 3, 5, 6, 10, 11 and 12). At each test location, corn was treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with a 5- to 8-day application interval for a total seasonal rate of 500 g a.i./ha. All applications were made using ground-based equipment.

Samples of corn forage and sweet corn ears (kernels plus cob with husks removed) were harvested at 0-day PHI and samples of corn stover and grain were harvested at 11- to 14-day PHIs. One trial for sweet corn and two trials for field corn were decline trials where samples were harvested at PHIs of 0-1, 3, 7, 9-10 and 13-14 days.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Corn forage	500	0	32	1.56	5.52	5.15	3.29	3.52	1.14
Corn stover		11-14	30	0.70	14.69	13.40	1.69	2.61	3.09
Corn grain		11-14	30	<0.01	0.020	0.018	<0.01	<0.01	<0.01
Sweet corn ears		0	18	<0.01	<0.01	<0.01	<0.01	<0.01	0

Crop Field Trials Used as Rotational Crop Data – Wheat and Sorghum **PMRA# 1661247**

Fifteen residue trials on wheat and twelve residue trials on sorghum were conducted (in NAFTA Growing Regions 2, 4, 5, 6, 7, 8 and 11). At each test location, wheat and sorghum were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application with a 14-day application interval for a total seasonal rate of 500 g a.i./ha. All applications were made using ground-based equipment.

Samples of wheat forage, hay, grain and straw were harvested at 12- to 15-day PHIs and samples of sorghum forage, grain and stover were harvested at 13- to 15-day PHIs. One trial each for wheat and sorghum was a decline trial where samples were harvested at PHIs of 0, 7, 14, 21 and 28 days.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat forage	500	14	30	0.052	3.03	2.91	0.610	0.788	0.688
Wheat grain			30	0.037	0.764	0.722	0.192	0.218	0.150
Wheat hay			32	0.280	5.51	5.41	1.66	2.19	1.75
Wheat straw			32	0.785	12.26	11.52	4.64	4.65	3.06
Sorghum forage	500	14	24	0.18	4.10	4.08	0.858	1.13	1.12
Sorghum grain			24	0.23	3.24	3.03	0.34	0.622	0.767
Sorghum stover			24	0.19	12.15	8.63	1.01	1.65	2.49

Crop Field Trials Used As Rotational Crop Data – Canola **PMRA# 1661254**

Eight residue trials on canola were conducted (in NAFTA Growing Regions 2, 5, 7 and 11). At each test location, canola was treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application for a total seasonal rate of 500 g a.i./ha. The interval between applications was 13 to 14 days. For all trials, the applications were made at BBCH growth stage 65 to 89 (BBCH 65: Full flowering: 50% of flowers on main raceme open; BBCH 89: Fully ripe). All applications were made using ground-based equipment.

Canola seed was harvested at a 12 to 14-day PHI at commercial maturity. One trial was a decline trial in which samples of canola seed were collected at PHIs of 0, 6, 12, 19 and 26 days following application.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Canola seeds	500	12-14	16	0.089	3.00	2.89	0.140	0.512	0.934

Crop Field Trials Used As Rotational Crop Data – Soybeans **PMRA# 1661216**

Twenty residue trials on soybeans were conducted (in NAFTA Growing Regions 2, 3, 4 and 5). At each test location, soybeans were treated with two foliar spray applications of AE C656948 500 SC at a rate of 250 g a.i./ha per application for a total seasonal rate of 500 g a.i./ha. All applications were made using ground-based equipment.

Each trial had two treated plots. In the treated plot from which the forage and hay were sampled, the 1st application was made at a BBCH growth stage between 14 (trifoliate leaf on the 4th node unfolded) and 75 (about 50% of pods reached final length [15–20 mm]). The 2nd application was made 5-7 days later, and forage and hay were harvested at a 6- to 7-day PHI at a target growth stage between BBCH 65 and 69. In the treated plots from which seed was sampled, the 1st application was made at a BBCH growth stage between 75 (about 50% of pods reached final length [15–20 mm]) and 88 (about 80% pods ripe, beans final color, dry and hard). The 2nd application was made 5-8 days later, with the exception of one trial that had a 14-day application interval. Seed was harvested from plot TRTDS at a 12- to 14-day PHI (except one trial with a 17-day PHI and one trial that cut the soybean plants at a 14-day PHI and sampled the seed the following day) at a target BBCH 89 growth stage. When necessary, hay was allowed to dry to commercial dryness prior to sampling. Two trials were decline trials where seed samples were harvested at PHIs of 0, 7, 21 and 28 days.

Commodity	Total Appl. Rate (g a.i./ha)	PHI (days)	Fluopyram Residue Levels (ppm)						
			n	Min	Max	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Soybean forage	500	7	40	0.320	6.19	5.70	2.53	2.62	1.48
Soybean hay			40	1.21	20.90	20.20	6.19	7.50	4.91
Soybean seed		14	40	<0.01	0.180	0.160	<0.01	0.021	0.036

Table 18g Residues in Processed Food and Feed

PROCESSED FOOD AND FEED - Potato	**PMRA# 1654380 (or 1661287)**
Test Site	One trial in NAFTA Growing Region 5
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	6 days
Processed Commodity	Average Processing Factor
Wet peel	4.3x
Chips	0.3x
Flakes	1.0x
Washed tubers	0.7x
Peeled tubers	0.2x
Cooked tubers	0.3x
PROCESSED FOOD AND FEED – Sugar beet	**PMRA# 1654379 (or 1661286)**
Test Site	One trial in NAFTA Growing Region 5
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	7 days
Processed Commodity	Average Processing Factor
Dried pulp	1.3x
Refined sugar	1.3x
Molasses	0.9x
PROCESSED FOOD AND FEED – Apple	**PMRA# 1654383 (or 1661291), 1654393 and 1654394**
North American Trials	
Test Site	One trial in NAFTA Growing Region 1
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	5 days
Processed Commodity	Average Processing Factor
Washed apples	0.7x
Peeled apples	0.03x
Dried apples	0.03x
Apple juice	0.4x
Applesauce	0.01x
Wet pomace	2.3x
EU Trials	
Test Site	Southern Europe (Southern France and Italy) and Northern Europe (Belgium and UK)
Treatment	Broadcast foliar applications
Rate	Four applications at 125 g a.i./ha for a total rate of 0.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	7 days
Processed Commodity	Average Processing Factor
Washed apples	0.7x

Peeled apples	0.25x
Dried apples	0.75x
Apple juice	0.1x
Applesauce	0.4x
Wet pomace	2.4x
Dried pomace	7.7x
PROCESSED FOOD AND FEED – Grape	**PMRA# 1599645, 1599646, 1599660 and 1599584**
North American Trials	
Test Site	One trial in NAFTA Growing Region 10
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	7 days
Processed Commodity	Average Processing Factor
Raisins	2.4x
Juice	0.5x
Washed berries	0.8x
Jelly	0.1x
EU Trials	
Test Site	Four trials in Southern and Northern France
Treatment	Broadcast foliar applications
Rate	Two applications at 250 g a.i./ha for a total rate of 0.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	3 days
Processed Commodity	Average Processing Factor
Washed berries	0.6x
Wet pomace	3.2x
Dried pomace	6.4x
Grape juice	No quantifiable residues
Wine	0.2x
Test Site	Southern Europe (One trial each in Spain, Portugal, Italy, Greece)
Treatment	Broadcast foliar applications
Rate	Two applications at 250 g a.i./ha for a total rate of 0.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	3 days
Processed Commodity	Average Processing Factor
Raisins	3.7x
PROCESSED FOOD AND FEED – Strawberry	**PMRA# 1599587, 1599659 and 1599658**
North American Trials	
Test Site	One trial in NAFTA Growing Region 10
Treatment	Broadcast foliar applications
Rate	Two applications at 250 g a.i./ha for a total rate of 0.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	0 day
Processed Commodity	Average Processing Factor
Washed fruit	0.7x
Washed and cooked (~ jam)	0.7x
EU Trials	
Test Site	Southern and Northern France, Belgium and Spain
Treatment	Broadcast foliar applications
Rate	Two applications at 250 g a.i./ha for a total rate of 0.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	1 day

Processed Commodity	Average Processing Factor
Washed fruit	0.8x
Preserve (incl. pasteurization)	0.3x
Jam	0.5x
PROCESSED FOOD AND FEED - Peanut	**PMRA# 1654372 (or 1661275)**
Test Site	One trial in NAFTA Growing Region 2
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	6 days
Processed Commodity	Average Processing Factor
Meal	0.2x
Refined oil	0.3x
Dry roasted peanuts	0.3x
Peanut butter	0.2x
PROCESSED FOOD AND FEED - Wheat	**PMRA# 1654374 (or 1661280)**
Test Site	One trial in NAFTA Growing Region 5
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	14 days
Processed Commodity	Average Processing Factor
Bran	2.7x
Flour	0.12x
Middlings	0.34x
Shorts	0.75x
Germ	2.4x
Aspirated grain fractions	70x
PROCESSED FOOD AND FEED – Field corn	**PMRA# 1654373 (or 1661276)**
Test Site	One trial in NAFTA Growing Region 5
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	12 days
Processed Commodity	Average Processing Factor
Wet milled starch	<0.4x
Wet-milled refined oil	0.6x
Grits	0.5x
Flour	0.9x
Meal	0.8x
Bran	2.6x
Dry-milled refined oil	<0.4x
Aspirated grain fractions	160x
PROCESSED FOOD AND FEED - Canola	**PMRA# 1654378 (or 1661285), 1654391 and 1654395**
North American Trials	
Test Site	One trial in NAFTA Growing Region 5
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	14 days
Processed Commodity	Average Processing Factor
Refined oil	0.01x
Meal	0.3x

EU Trials	
Test Site	Southern Europe (Southern France and Italy) and Germany
Treatment	Broadcast foliar applications
Rate	Two applications at 125 g a.i./ha for a total rate of 0.25 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	34-57 days
Processed Commodity	Average Processing Factor
Refined oil	1.1x
Screwpressed oil	1.4x
Crude oil	1.4x
Extracted meal	0.8x
Solvent extracted oil	1.4x
Pomace	0.9x
PROCESSED FOOD AND FEED - Soybeans	**PMRA# 1654375 (or 1661282)**
Test Site	One trial in NAFTA Growing Region 5
Treatment	Broadcast foliar applications
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	13 days
Processed Commodity	Average Processing Factor
Meal	0.05x
Hulls	1.3x
Refined oil	0.02x
Flour	0.04x
Soy milk	0.01x
Aspirated grain fractions	223x
PROCESSED FOOD AND FEED - Cotton	**PMRA# 1654376 (or 1661283)**
Test Site	One trial in NAFTA Growing Region 4
Treatment	Broadcast applications to bare ground; cotton was planted with a PBI of 12 days
Rate	Two applications at 1250 g a.i./ha for a total rate of 2.5 kg a.i./ha/season
End-use product	AE C656948 500 SC
Preharvest interval	Samples were collected at commercial harvest stage
Processed Commodity	Average Processing Factor
Meal	Residues were <LOQ in cotton seed and all processed commodities; processing factors could not be determined.
Hulls	
Refined oil	

Table 18h Livestock Feeding

LIVESTOCK FEEDING – Dairy cattle	**PMRA# 1599761**
Four treatment groups of three dairy cows each were dosed orally with fluopyram, via double-coated gelatine capsules, for 29 consecutive days at dose levels corresponding to residue intake in diet of 1 ppm, 10 ppm, 30 ppm and 100 ppm dry feed. One cow served as a control. A depuration study was conducted for the 100 ppm dosing group in which animals were sacrificed 7, 14 or 21 days after withdrawal of the dose. (One animal was excluded from the 100 ppm dose group based on reduced feed intake and no data for this animal are reported.) Duplicate milk samples from the animals were taken before the 1st dosing (Day -7) as well as on Day 1, 2, 4, 8, 10, 13, 17, 21, 24, 26 and 29 after the 1st administered dose. Milk was additionally collected from animals in the depuration study for up to Day 50. The evening milk for each cow was frozen overnight and combined with the following morning milk sample. In addition, additional milk samples from the 100 ppm dose group were collected (Day 20/21) for processing into milk whey and milk fat (cream). Animals were sacrificed within 24 hours after the final dose, and samples of liver, muscle, kidney and fat (perirenal, subcutaneous and mesenteric) were collected for analysis.	

The depuration study showed that residues of fluopyram and AE C656948-benzamide in milk and tissues decreased following the withdrawal period. Total residues of olefines in liver and kidney also decreased and total residues of olefines in muscle were below the LOQ. Total residues of olefines in subcutaneous, perirenal and mesenteric fat increased during the depuration period.

Matrix	**Maximum Residues of Fluopyram and Metabolites [ppm]**			
	1.5 ppm dose group	**14.4 ppm dose group**	**44.1 ppm dose group**	**133.1 ppm dose group**
Fluopyram				
Milk (Day 4 to end)	<0.01	<0.01-0.02 (mean = 0.01)	0.02-0.09 (mean = 0.03)	0.06-0.17 (mean = 0.10)
Skim milk	N/A	N/A	N/A	0.02
Cream	N/A	N/A	N/A	1.4
Fat	<0.01	0.07	0.33	0.71
Kidney	<0.01	<0.01	0.05	0.08
Liver	0.26	0.98	2.8	4.0
Muscle	<0.01	<0.01	0.04	0.03
AE C656948-benzamide				
Milk (Day 8 to end)	0.01-0.09 (mean = 0.02)	0.15-0.37 (mean = 0.22)	0.40-0.77 (mean = 0.54)	1.1-1.9 (mean = 1.5)
Skim milk	N/A	N/A	N/A	1.5
Cream	N/A	N/A	N/A	0.98
Fat	0.01	0.33	0.45	1.1
Kidney	0.03	0.38	0.88	1.6
Liver	0.10	1.9	3.2	7.0
Muscle	0.02	0.44	0.79	1.5
Combined Residues of Fluopyram and AE C656948-benzamide				
Milk (Day 8 to end)	<0.02-<0.10 (mean = 0.03)	<0.16-0.39 (mean = 0.23)	0.42-0.80 (mean = 0.57)	1.2-2.0 (mean = 1.6)
Fat	<0.02	0.37	0.78	1.6
Kidney	<0.04	<0.39	0.93	1.7
Liver	0.36	2.3	5.3	10.9
Muscle	<0.03	<0.45	0.83	1.5
AE C656948-olefines				
Milk (Day 8 to end)	<0.02	≤0.02	<0.02-0.05 (mean = 0.02)	0.07-0.14 (mean = 0.10)
Skim milk	N/A	N/A	N/A	<0.02
Cream	N/A	N/A	N/A	1.3
Fat	<0.02	0.12	0.32	0.94
Kidney	<0.02	<0.02	0.04	0.15
Liver	<0.02	0.06	0.13	0.58
Muscle	<0.02	<0.02	0.03	0.04

LIVESTOCK FEEDING – Laying Hen **PMRA# 1599760**

Four treatment groups of 12 laying hens each were dosed orally with fluopyram, via feed, for 28 consecutive days at dose levels corresponding to 0.05 ppm, 0.50 ppm, 1.5 ppm and 5.0 ppm feed. Nine hens were dosed at the 0 ppm level to serve as the control group. A depuration study was conducted for the 5.0 ppm dosing group in which animals were sacrificed 8, 13 or 21 days after withdrawal of the dose.

Eggs were collected from each dose subgroup daily during the dosing period, and pooled for each subgroup per sampling day, on study days -13, -6, -1, 0, 1, 2, 5, 7, 9, 12, 14, 16, 21, 23, 26 and 28. Eggs were additionally collected from animals in the depuration study for up to Day 49. Animals were sacrificed 3-7 hours after the final dose, and samples of liver (entire organ), muscle, and overlaying skin together with any associated fat (and abdominal fat) were collected for analysis.

The depuration study showed that residues of fluopyram, AE C656948-benzamide and olefines in eggs and poultry tissues decreased following the withdrawal period.

Matrix	Maximum Residues of Fluopyram and Metabolites [ppm]			
	0.05 ppm dose group	0.49 ppm dose group	1.6 ppm dose group	4.8 ppm dose group
Fluopyram				
Egg (Day 21 to end)	<0.01	<0.01	<0.01	<0.01
Skin with fat	<0.01	<0.01	<0.01	<0.01
Liver	<0.01	<0.01	<0.01	<0.01
Muscle	<0.01	<0.01	<0.01	<0.01
AE C656948-benzamide				
Egg (Day 21 to end)	<0.01	0.07-0.09 (mean = 0.08)	0.20-0.23 (mean = 0.21)	0.64-0.76 (mean = 0.71)
Skin with fat	<0.01	0.04	0.11	0.63
Liver	0.02	0.16	0.43	1.6
Muscle	<0.01	0.04	0.10	0.33
Combined Residues of Fluopyram and AE C656948-benzamide				
Egg (Day 21 to end)	<0.02	<0.08-<0.10 (mean = 0.09)	<0.21-<0.24 (mean = 0.22)	<0.65-<0.77 (mean = 0.72)
Skin with fat	<0.02	<0.05	<0.12	<0.64
Liver	<0.03	<0.17	<0.44	<1.6
Muscle	<0.02	<0.05	<0.11	<0.34
AE C656948-olefines				
Egg (Day 21 to end)	<0.02	<0.02	<0.02	<0.02-0.02
Skin with fat	<0.02	<0.02	0.03	0.08
Liver	<0.02	<0.02	<0.02	0.02
Muscle	<0.02	<0.02	<0.02	0.06

Table 19 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT Primary crops and rotational crops	Fluopyram
RESIDUE DEFINITION FOR RISK ASSESSMENT Crop Groups 6 (Legume Vegetables) and 20 (Oilseeds) All other crops	Fluopyram including the metabolite fluopyram-benzamide (expressed as parent equivalent) Fluopyram
METABOLIC PROFILE IN DIVERSE CROPS	Similar in grapes, potatoes, beans, red bell peppers
ANIMAL STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT Ruminants and poultry	Fluopyram including the metabolite fluopyram-benzamide (expressed as parent equivalent)
RESIDUE DEFINITION FOR RISK ASSESSMENT Poultry tissues and eggs Ruminant tissues and milk	Fluopyram including the metabolites fluopyram-benzamide and fluopyram-olefines (total of 2 isomers) (expressed as parent equivalent) Fluopyram including the metabolites fluopyram-benzamide, fluopyram-olefines (total of 2 isomers) and fluopyram-7-hydroxy (expressed as parent equivalent)

METABOLIC PROFILE IN ANIMALS		Similar in goat, hen, rat	
FAT SOLUBLE RESIDUE		No	
DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic dietary risk ADI = 0.012 mg/kg bw/day Estimated chronic drinking water concentration = 104 µg a.i./L	All infants < 1 year	3.9	63.8
	Children 1–2 years	6.3	33.4
	Children 3–5 years	3.9	29.3
	Children 6–12 years	2.0	19.5
	Youth 13–19 years	0.8	14.0
	Adults 20–49 years	0.8	17.8
	Adults 50+ years	1.0	18.9
	Females 13–49 years	0.8	17.8
	Total population	1.3	19.6
	POPULATION	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
Basic acute dietary exposure analysis, 95th percentile Estimated acute drinking water concentration = 106 µg a.i./L ARfD = 0.5 mg/kg bw	All infants < 1 year	7.0	9.1
	Children 1–2 years	8.8	9.8
	Children 3–5 years	7.5	8.4
	Children 6–12 years	5.3	5.8
	Youth 13–19 years	3.5	3.9
	Adults 20–49 years	2.8	3.3
	Adults 50+ years	2.2	2.8
	Females 13–49 years	2.8	3.3
	Total population	4.4	5.0
Refined chronic cancer dietary risk Q_1* = 0.0172 (mg/kg bw/day)$^{-1}$ Estimated chronic drinking water concentration = 2.93 µg a.i./L	**POPULATION**	**ESTIMATED RISK Adjusted for Limited 3-Year Application Period**	
		Food and Water	
	Total population	1×10^{-6}	

Table 20 Summary of Physico-Chemical Properties of Fluopyram Relevant to the Environment

Parameter	Values	Interpretation
Water solubility (at 20°C)	pH 4 → 15 mg/L pH 7 → 16 mg/L pH 9 → 15 mg/L	soluble under environmentally relevant pH conditions
Vapour pressure/volatility	20°C → 1.2×10^{-6} Pa 25°C → 3.1×10^{-6} Pa 50°C → 2.9×10^{-4} Pa	non-volatile under field conditions
Henry's Law Constant	20°C→ 2.98×10^{-5} Pa m^3 mol^{-1}	low potential for volatilization from moist soil and water surfaces

Parameter	Values	Interpretation
UV absorption	< 292 nm	low potential for phototransformation
pK_a (at 23°C)	0.5	does not dissociate under environmentally relevant pH conditions
K_{ow}/log K_{ow}	pH 6.5 → 2060 / 3.3	potential for bioaccumulation
Stability of compound at room temperature	Stable, no decomposition	

Table 21 Fate and Behaviour in the Terrestrial Environment

Study	Label/Product	System	DT_{50} (days)	DT_{90} (days)	Kinetic Model
Soils					
Hydrolysis	phenyl	stable to hydrolysis under acidic, neutral and alkaline conditions			
Soil Photolysis	phenyl	stable to photolysis in soils			
Aerobic soil	phenyl	Hohenseh silt loam	221	735	SFO
		AXXa sandy loam	231	769	SFO
		Wurmwiese loam	339	>1000	SFO
		Allla loam	165	549	SFO
		Porterville sandy loam	746	>1000	SFO
		Springfield silt clay loam	654	>1000	DFOP
	pyridyl	Hohenseh silt loam	210	697	SFO
		AXXa sandy loam	464	>1000	SFO
		Wurmwiese sandy loam	250	829	SFO
		Dollendorf clay loam	162	538	SFO
		Porterville sandy loam	561	>1000	SFO
		Springfield silty clay loam	583	>1000	DFOP
Anaerobic soil	phenyl	Hoefchen silt loam	>1000	>1000	SFO
	pyridyl	Hohenseh silt loam	>1000	>1000	SFO
Field studies: Europe	dissipation: fluopyram 250 SC	Burscheid, GER [silt loam]	145	>1000	DFOP
		Little Shelford, UK [sandy loam]	164	>1000	DFOP
		Staffanstorp, Sweden [loam]	386	>1000	SFO
		Vatteville, France [silt loam]	318	>1000	DFOP
		Vilobi d'Onyar, Spain [loam]	147	487	SFO
		Albaro, Italy [silt loam]	21	512	DFOP
	accumulation: fluopyram 250SC	Monheim, GER [sandy loam]	end of 1st year:29% of 0-day 1st application end of 2nd year:57% of 0-day 2nd application		
		Tarascon, France [silt loam]	end of 1st year: 53% of 0-day 1st application end of 2nd year: 59% of 0-day 2nd application		
Field studies: US	dissipation/ accumulation: AE C656948 500SC	Washington [sandy loam]	163	DT_{75}:816 DT_{90} >1000	DFOP
		New York [loamy sand]	539	DT_{75}: >1000 DT_{90}: >1000	DFOP
		North Dakota [loam]	83	DT_{75}: >1000 DT_{90}: >1000	DFOP
		Georgia [loamy sand]	24	DT_{75}: 521 DT_{90}: >1000	DFOP
		California [sandy loam]	174	DT_{75}:688 DT_{90}: >1000	DFOP

Study	Label/Product	System	DT_{50} (days)	DT_{90} (days)	Kinetic Model
Adsorption/ desorption	AE C656948	Laacherhof AXXa(sandy loam)	$K_{d(ad)}$: 3.80 $K_{oc(ad)}$: 292	$K_{d(des)}$: 8.27 $K_{oc(des)}$: 636	
		Hoefchen a. Hohenseh(silt loam)	$K_{d(ad)}$: 8.37 $K_{oc(ad)}$: 322	$K_{d(des)}$: 13.15 $K_{oc(des)}$:506	
		Laacherhof Wurmwiese(loam)	$K_{d(ad)}$: 5.59 $K_{oc(ad)}$: 266	$K_{d(des)}$: 9.33 $K_{oc(des)}$:444	
		Pikeville(loamy sand)	$K_{d(ad)}$: 3.16 $K_{oc(ad)}$: 288	$K_{d(des)}$: 6.32 $K_{oc(des)}$:575	
		Stilwell(clay loam)	$K_{d(ad)}$: 5.06 $K_{oc(ad)}$: 460	$K_{d(des)}$: 9.17 $K_{oc(des)}$:834	
	AE C656948-7-hydroxy	AIIIa(loam)	$K_{d(ad)}$: 1.03 $K_{oc(ad)}$: 94	$K_{d(des)}$: 3.54 $K_{oc(des)}$:322	
		AXXa(sandy loam)	$K_{d(ad)}$:1.36 $K_{oc(ad)}$: 91	$K_{d(des)}$: 3.78 $K_{oc(des)}$:252	
		Hoefchen(silt loam)	$K_{d(ad)}$: 2.54 $K_{oc(ad)}$:159	$K_{d(des)}$: 7.16 $K_{oc(des)}$:447	
		Wurmwiese(sandy loam)	$K_{d(ad)}$: 1.38 $K_{oc(ad)}$: 86	$K_{d(des)}$: 3.88 $K_{oc(des)}$:243	

Table 22 Fate and Behaviour in the Aquatic Environment

Study	Label	System	DT_{50} (days)	DT_{90} (days)	Kinetic model
Aquatic systems					
Hydrolysis		stable to hydrolysis under acidic, neutral and alkaline conditions			
Water photolysis	phenyl and pyridyl	buffer solution (pH 7)	21 and 25 52 and 63[a] 81 and 97[b]		SFO
	phenyl and pyridyl	natural water/sediment	21, 87[s] and 135[b]		SFO
Aerobic aquatic	phenyl	Angleweiher -water phase	25	280	DFOP
		Angleweiher-total system	1190	3960	SFO
		Lawrence-water phase	14	220	DFOP
		Lawrence-total system	1000	3300	SFO
	pyridyl	Angleweiher-water phase	26	290	DFOP
		Angleweiher-total system	1470	4900	SFO
		Lawrence-water phase	17	220	DFOP
		Lawrence-total system	650	2150	SFO
Anaerobic aquatic	phenyl	Lawrence-water phase	4	89	DFOP
		Lawrence-total system	1580	5240	SFO
	pyridyl	Lawrence-water phase	5	79	FOMC
		Lawrence-total system	1410	4680	SFO

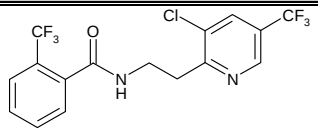
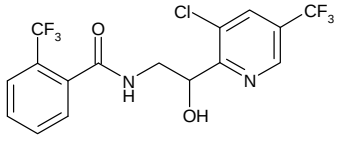
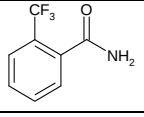
[a]equivalent days of sunlight in Phoenix, Arizona
[b] Equivalent days of sunlight in Athens, Greece

Table 23 Maximum Concentrations of Transformation Products in Soil and Water

Property	Transformation products	
	Major	Minor
Soil		
Hydrolysis	None	None
Phototransformation	None	None
Aerobic Biotransformation	None	AE C656948-7-hydroxy (4.2% AR)
		AE C656948- pyridyl-carboxylic acid (0.7% AR)
		AE C656948-methyl-sulfoxide (1.0% AR)
		AE C656948-benzamide (1.1% AR)
Anaerobic Biotransformation	None	None
Field dissipation: Europe	not determined	
Field dissipation: US	AE C656948-benzamide (19%)*	AE C656948-7-hydroxy (3%)**
	AE C656948- pyridyl-carboxylic acid (16%)*	AE C656948-benzamide** AE C656948- pyridyl-carboxylic acid**
Water		
Hydrolysis	None	none
Phototransformation	pH 7 buffer: AE C656948-lactam (13% AR)	none
	natural water/sediment system: none	AE C656948-lactam (1.2% AR)
Aerobic Biotransformation	none	none
Anaerobic Biotransformation	none	none

AR: applied radioactivity
( ): % of 0-day concentration
*detected only at the California site
** detected at sites relevant to Canadian field use conditions

Table 24 Structure and Properties of Parent Compound and Transformation Products

Common name	Chemical name (CAS)	Structure	Formula and molar mass
Fluopyram	Benzamide, N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)- (9CI)		$C_{16}H_{11}ClF_6N_2O$ 396.72 g/mol
Fluopyram - 7-hydroxy	N-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]-2-hydroxyethyl}-2-(trifluoromethyl)benzamide		$C_{16}H_{11}ClF_6N_2O_2$ 412.72 g/mol
Fluopyram-benzamide	2-trifluoromethyl benzamide		$C_8H_6F_3NO$ 189.15 g/mol

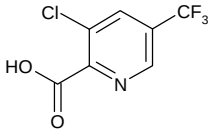
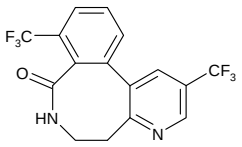
Common name	Chemical name (CAS)	Structure	Formula and molar mass
Fluopyram - pyridyl-carboxylic acid	[3-chloro-5-(trifluoromethyl)pyridin-2-carboxylic acid		$C_7 H_3 Cl F_3 N O_2$ 225.26 g/mol
Fluopyram-lactame	2,9-bis(trifluoromethyl)-6,7-dihydropyrido[2,3-e][2]benzazocin-8(5H)-one		$C_{16} H_{10} F_6 N_2 O$ 360.26 g/mol

Table 25 Screening Level EECs* (Luna Privilege)

Soil**	Water***	
	15 cm depth	80 cm depth
0.22 mg a.i./kg soil	0.33 mg a.i./L water	0.062 mg a.i./L water

*based on 2 application of 250 g a.i./ha each with a cumulative application rate 497.76 g
**top 30 cm soil depth and a soil bulk density of 1.5 g/cm^3
*** cumulative application of 499.18 g a.i./ha based on a half-life of 1470 days

Table 26 Level 1 Aquatic Eco-Scenario Modelling EECs for Fluopyram in a Water Body of 0.15 m Deep Excluding Spray Drift

Use pattern	EEC (µg a.i./L)					
	Peak	96-hour	21-day	60-day	90-day	Yearly
2 × 0.25 kg a.i./ha, at 7-day intervals						
Potato-PEI	299	290	261	253	252	244

[1]Vulnerable scenario used in this Level 1 aquatic eco-scenario modelling.

Table 27 EECs in Vegetation and Insects after a Direct Over-Spray[1] (Luna Privilege)

Matrix	EEC[a] (mg a.i./kg fw) (Max Residues)	Fresh/Dry Weight Ratios	EEC Direct Overspray (mg a.i./kg dw) (Max Residues)	EEC (Direct Overspray) (mg a.i./kg dw) (Mean Residues)
Short range grass	86.4383	3.3[b]	285.2465	101.3026
Leaves and leafy crops	48.8730	11[b]	537.6031	177.7200
Long grass	39.5830	4.4[b]	174.1652	56.8704
Forage crops	48.8730	5.4[b]	263.9143	87.2444
Small insects	21.0032	3.8[c]	79.8123	44.5107
Pods with seeds	5.2508	3.9[c]	20.4783	9.7666
Large insects	5.2508	3.8[c]	19.9532	9.5161
Grain and seeds	5.2508	3.8[c]	19.9532	9.5161
Fruit	5.2508	7.6[c]	39.9064	19.0323

[1] based on direct over-spray of a cumulative application rate of 403.909 g a.i./ha and a default half-life of 10 days)
[a] based on correlations reported by Hoerger and Kenaga (1972) and Kenaga (1973)
[b] fresh to dry weight ratios from Harris (1975)
[c] fresh to dry weight ratios from Spector (1956)

Table 28 Effects on Terrestrial Organisms

Organism	Exposure	Test Substance	End-Point Value	Degree of Toxicity	PMRA #
Invertebrates					
Earthworm (*Eisenia fetida andrei)*	14-d acute	AE C656948	LC_{50}: >1000 mg a.i./kg dw soil NOAEC: 100 mg a.i./kg dw soil EC_{50}: >1000 mg a.i./kg dw soil	N/A	1599606
	14-d acute	Luna Privilege G	LC_{50}: >415 mg a.i/kg dw soil EC_{50}: >415 mg a.i./kg dw soil NOAEC: 73.87a.i./kg dw soil	N/A	1599293
	reproduction (number of juveniles)	Luna Privilege G	EC_{50}: >20.3 mg a.i./kg dw soil; NOAEC: 11.4 mg a.i./kg dw soil	N/A	1599294 1599589
Honeybees (*Apis mellifera* L.)	48-h acute oral	AE C656948	LC_{50}: >102.3 µg a.i./bee NOAEL: 102.3 µg a.i./bee LOAEL: >102.3 µg a.i./bee	relatively nontoxic	1599733
	48-h acute contact	AE C656948	LD_{50}: >100 µg a.i/bee NOAEL: 100 µg a.i/bee LOAEL: >100 µg a.i./bee	relatively nontoxic	
	48-h acute contact and Oral	Luna Privilege G	Contact: LD_{50}: >83.2 µg a.i./bee NOAEL: 83.2 µg a.i./bee LOAEL: >83.2 µg a.i./bee Oral: LC_{50}: >89 µg a.i./bee NOAEL: 89 µg a.i./bee LOAEL: >89 µg a.i./bee	relatively nontoxic	1599290
Parasitic wasp *(Aphidius rhopalosiphi)*	acute	Luna Privilege G	LR_{50}: >1008 g a.i./ha	N/A	1599729 1599291
	chronic (reproduction)		$ER_{50:}$ >1008 g a.i./ha	N/A	
Predatory mite *(Typhlodromus pyri)*	acute	Luna Privilege G	LR_{50}: >1008 g a.i./ha	N/A	1599727 1599292
	Chronic (reproduction)		NOAEL:1008 g a.i./ha	N/A	
Other soil invertebrates					
Rove beetle (*Aleochara bilineata)*	chronic (reproduction)	Luna Privilege G	ER_{50}: >1008 g a.i./ha	N/A	1599634 1599295
Soil mite *Hypoaspis aculeifer* (Acari laelapidae)	14-d reproduction test	Luna Privilege G	LC_{50} > 415 mg a.i /kg dw soil NOEC: 415 mg a.i /kg dw soil	N/A	1599296
Springtail *Folsomia candida* (Collembola isotomidae)	chronic (reproduction)	Luna Privilege G	NOEC: 103.7 mg a.i./kg dw soil	N/A	1599297
Birds					
Bobwhite quail (*Colinus viriginianus*)	acute	AE C656948	LD_{50}: >2000 mg a.i./kg bw NOAEL: <500 mg a.i./kg bw	practically non-toxic	1599536
	dietary	AE C656948	LC_{50}: >4785 mg a.i./kg diet LD_{50}: 1845.4 mg a.i./kg bw/day LOAEC: 279 mg a.i./kg diet NOAEC: <279 mg a.i./kg diet	practically non-toxic	1599554

Organism	Exposure	Test Substance	End-Point Value	Degree of Toxicity	PMRA #
	reproduction	AE C656948	NOAEC: 46.7 mg a.i./kg diet (survival body weight) NOAEL: 4.12 mg a.i./kg bw/day LOAEC: 75.7 mg a.i./kg diet LOAEL: 6.8 mg a.i./kg bw/day	N/A	1599605
Mallard duck (*Anas platyrhynchos*)	dietary	AE C656948	LC_{50}: >4604.5 mg a.i./kg diet LD_{50}: 1642.7 mg a.i./kg bw/day NOAEC: 2307.1 mg a.i./kg diet LOAEC: 4604.5 mg a.i./kg diet	practically non-toxic	1599600
	reproduction	AE C656948	NOAEC: 183 mg a.i./kg diet (survivor weights) NOAEL: 18.46 mg a.i./kg bw/day LOAEC: 428 mg a.i./kg diet	N/A	1599731
Mammals					
Rat	acute oral	AE C 656948, Luna Privilege	LD_{50}: >2000 mg a.i./kg bw	practically non-toxic	
	dietary	AE C 656948	NOAEL: 12.5 mg a.i./kg bw/d		
	reproduction	AE C 656948	NOAEL: 13.9 mg a.i./kg bw/d		
Vascular plants					
Vascular plant	seedling emergence	Luna Privilege G	**Monocot**, most sensitive: none EC_{25}: > 500 g a.i./ha **Dicot**: most sensitive: Buckwheat (Biomass) EC_{25}: >500 g a.i./ha	N/A	1599302 1599591
	vegetative vigour	Luna Privilege G	**Monocot**, most sensitive: none EC_{25}: > 250 g a.i./ha **Dicot**: most sensitive: none EC_{25}: >250g a.i./ha	N/A	1599301 1599590

Table 29 Screening Level Risk Assessment to Terrestrial Organisms (Luna Privilege)

Organism	Exposure	Test Substance	Tox Value for RQ	EEC	RQ
Earthworm (*E. fetida)*	acute	Luna Privilege	LC_{50}×0.5: 207.5 mg a.i./kg dw soil*	0.22 mg a.i./kg soil	0.001
	reproduction	Luna Privilege	NOAEC: 11.4 mg a.i./kg dw soil	0.22 mg a.i./kg soil	0.02
Honeybees (*A. mellifera* L.)	acute contact	Luna Privilege	LD_{50}: 93.2 kg a.i./ha**	0.4039 kg a.i./ha	0.004
Predatory mite *(T. pyri)*	acute	Luna Privilege	LR_{50}: >1008 g a.i./ha	403.9 g a.i./ha	<0.40
	chronic (reproduction)	Luna Privilege	NOAEL: 1008 g a.i./ha	403.9 g a.i./ha	0.40

* with an uncertainty factor of two

** LD_{50} of >83.2 µg a.i./bee converted to >93.2 kg a.i./ha (based on conversion factor of 1.12 to kg per hectare according to Atkins *et al.*(1981)

Table 30 Screening Level Risk Assessment to Wild Birds

Effects	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	200.00*	Insectivore (small insects)	20.35	0.10
Reproduction	4.12	Insectivore (small insects)	20.35	4.94
Medium Sized Bird (0.1 kg)				

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

* based on an uncertainty factor of 10

Table 31 Expanded Screening Level Reproductive Risk Assessment to Wild Birds for On-Field and Off-Field Scenarios (Luna Privilege)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)		On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)																		
Reproduction	4.12	Insectivore (small insects)	20.35	4.94	15.06	3.66	12.01	2.91	1.22	0.30	11.35	2.75	8.40	2.04	6.70	1.63	0.68	0.17
	4.12	Granivore (grain and seeds)	5.09	1.23	3.77	0.91	3.00	0.73	0.31	0.07	2.43	0.59	1.80	0.44	1.43	0.35	0.15	0.04
	4.12	Frugivore (fruit)	10.18	2.47	7.53	1.83	6.00	1.46	0.61	0.15	4.85	1.18	3.59	0.87	2.86	0.70	0.29	0.07
Medium Sized Bird (0.1 kg)																		
Reproduction	4.12	Insectivore (small insects)	15.88	3.86	11.75	2.85	9.37	2.27	0.95	0.23	8.86	2.15	6.55	1.59	5.23	1.27	0.53	0.13
	4.12	Insectivore (large insects)	3.97	0.96	2.94	0.71	2.34	0.57	0.24	0.06	1.89	0.46	1.40	0.34	1.12	0.27	0.11	0.03
	4.12	Granivore (grain and seeds)	3.97	0.96	2.94	0.71	2.34	0.57	0.24	0.06	1.89	0.46	1.40	0.34	1.12	0.27	0.11	0.03
	4.12	Frugivore (fruit)	7.94	1.93	5.88	1.43	4.69	1.14	0.48	0.12	3.79	0.92	2.80	0.68	2.23	0.54	0.23	0.06
Large Sized Bird (1 kg)																		
Reproduction	4.12	Insectivore (small insects)	4.64	1.13	3.43	0.83	2.74	0.66	0.28	0.07	2.59	0.63	1.91	0.46	1.53	0.37	0.16	0.04
	4.12	Insectivore (large insects)	1.16	0.28	0.86	0.21	0.68	0.17	0.07	0.02	0.55	0.13	0.41	0.10	0.33	0.08	0.03	0.01
	4.12	Granivore (grain and seeds)	1.16	0.28	0.86	0.21	0.68	0.17	0.07	0.02	0.55	0.13	0.41	0.10	0.33	0.08	0.03	0.01
	4.12	Frugivore (fruit)	2.32	0.56	1.72	0.42	1.37	0.33	0.14	0.03	1.11	0.27	0.82	0.20	0.65	0.16	0.07	0.02
	4.12	Herbivore (short grass)	16.57	4.02	12.26	2.98	9.78	2.37	0.99	0.24	5.89	1.43	4.36	1.06	3.47	0.84	0.35	0.09
	4.12	Herbivore (long grass)	10.12	2.46	7.49	1.82	5.97	1.45	0.61	0.15	3.30	0.80	2.45	0.59	1.95	0.47	0.20	0.05
	4.12	Herbivore (forage crops)	15.33	3.72	11.35	2.75	9.05	2.20	0.92	0.22	5.07	1.23	0.30	0.07	2.99	0.73	0.30	0.07

EDE: mg a.i./kg bw

Table 32 Refined Assessment of Reproductive Risk to Wild Birds for On-Field and Off-Field Scenarios (Luna Privilege)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)		On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)																		
Reproduction	6.8	Insectivore (small insects)	20.35	2.99	15.06	2.21	12.01	1.77	1.22	0.18	11.35	1.67	8.40	1.24	6.70	0.98	0.68	0.10
	6.8	Granivore (grain and seeds)	5.09	0.75	3.77	0.55	3.00	0.44	0.31	0.04	2.43	0.36	1.80	0.26	1.43	0.21	0.15	0.02
	6.8	Frugivore (fruit)	10.18	1.50	7.53	1.11	6.00	0.88	0.61	0.09	4.85	0.71	3.59	0.53	2.86	0.42	0.29	0.04
Medium Sized Bird (0.1 kg)																		

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)		On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Reproduction	6.8	Insectivore (small insects)	15.88	2.34	11.75	1.73	9.37	1.38	0.95	0.14	8.86	1.30	6.55	0.96	5.23	0.77	0.53	0.08
	6.8	Insectivore (large insects)	3.97	0.58	2.94	0.43	2.34	0.34	0.24	0.04	1.89	0.28	1.40	0.21	1.12	0.16	0.11	0.02
	6.8	Granivore (grain and seeds)	3.97	0.58	2.94	0.43	2.34	0.34	0.24	0.04	1.89	0.28	1.40	0.21	1.12	0.16	0.11	0.02
	6.8	Frugivore (fruit)	7.94	1.17	5.88	0.86	4.69	0.69	0.48	0.07	3.79	0.56	2.80	0.41	2.23	0.33	0.23	0.03
Large Sized Bird (1 kg)																		
Reproduction	6.8	Insectivore (small insects)	4.64	0.68	3.43	0.50	2.74	0.40	0.28	0.04	2.59	0.38	1.91	0.28	1.53	0.22	0.16	0.02
	6.8	Insectivore (large insects)	1.16	0.17	0.86	0.13	0.68	0.10	0.07	0.01	0.55	0.08	0.41	0.06	0.33	0.05	0.03	0.00
	6.8	Granivore (grain and seeds)	1.16	0.17	0.86	0.13	0.68	0.10	0.07	0.01	0.55	0.08	0.41	0.06	0.33	0.05	0.03	0.00
	6.8	Frugivore (fruit)	2.32	0.34	1.72	0.25	1.37	0.20	0.14	0.02	1.11	0.16	0.82	0.12	0.65	0.10	0.07	0.01
	6.8	Herbivore (short grass)	16.57	2.44	12.26	1.80	9.78	1.44	0.99	0.15	5.89	0.87	4.36	0.64	3.47	0.51	0.35	0.05
	6.8	Herbivore (long grass)	10.12	1.49	7.49	1.10	5.97	0.88	0.61	0.09	3.30	0.49	2.45	0.36	1.95	0.29	0.20	0.03
	6.8	Herbivore (forage crops)	15.33	2.25	11.35	1.67	9.05	1.33	0.92	0.14	5.07	0.75	3.75	0.55	2.99	0.44	0.30	0.04

EDE: mg a.i./kg bw

Table 33 Screening Level Risk Assessment to Mammals (Luna Privilege)

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

*based on an uncertainty factor of 10

Table 34 Expanded Screening Level Assessment of Reproductive Risk to Mammals with Same Endpoints (Luna Privilege)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Mammal (0.015 kg)																		
Reproduction	13.90	Insectivore (small insects)	11.71	0.84	8.66	0.62	6.91	0.50	0.70	0.05	6.53	0.47	4.83	0.35	3.85	0.28	0.39	0.03
	13.90	Granivore (grain and seeds)	2.93	0.21	2.17	0.16	1.73	0.12	0.18	0.01	1.40	0.10	1.03	0.07	0.82	0.06	0.08	0.01
	13.90	Frugivore (fruit)	5.85	0.42	4.33	0.31	3.45	0.25	0.35	0.03	2.79	0.20	2.07	0.15	1.65	0.12	0.17	0.01
Medium Sized Mammal (0.035 kg)																		
Reproduction	13.90	Insectivore (small insects)	10.26	0.74	7.59	0.55	6.05	0.44	0.62	0.04	5.72	0.41	4.23	0.30	3.38	0.24	0.34	0.02
	13.90	Insectivore (large insects)	2.57	0.18	1.90	0.14	1.51	0.11	0.15	0.01	1.22	0.09	0.91	0.07	0.72	0.05	0.07	0.01
	13.90	Granivore (grain and seeds)	2.57	0.18	1.90	0.14	1.51	0.11	0.15	0.01	1.22	0.09	0.91	0.07	0.72	0.05	0.07	0.01
	13.90	Frugivore (fruit)	5.13	0.37	3.80	0.27	3.03	0.22	0.31	0.02	2.45	0.18	1.81	0.13	1.44	0.10	0.15	0.01
	13.90	Herbivore (short grass)	36.67	2.64	27.14	1.95	21.64	1.56	2.20	0.16	13.02	0.94	9.64	0.69	7.68	0.55	0.78	0.06
	13.90	Herbivore (long grass)	22.39	1.61	16.57	1.19	13.21	0.95	1.34	0.10	7.31	0.53	5.41	0.39	4.31	0.31	0.44	0.03
	13.90	Herbivore (forage crops)	33.93	2.44	25.11	1.81	20.02	1.44	2.04	0.15	11.22	0.81	8.30	0.60	6.62	0.48	0.67	0.05
Large Sized Mammal (1 kg)																		
Reproduction	13.90	Insectivore (small insects)	5.48	0.39	4.06	0.29	3.24	0.23	0.33	0.02	3.06	0.22	2.26	0.16	1.80	0.13	0.18	0.01
	13.90	Insectivore (large insects)	1.37	0.10	1.01	0.07	0.81	0.06	0.08	0.01	0.65	0.05	0.48	0.03	0.39	0.03	0.04	0.00
	13.90	Granivore (grain and seeds)	1.37	0.10	1.01	0.07	0.81	0.06	0.08	0.01	0.65	0.05	0.48	0.03	0.39	0.03	0.04	0.00
	13.90	Frugivore (fruit)	2.74	0.20	2.03	0.15	1.62	0.12	0.16	0.01	1.31	0.09	0.97	0.07	0.77	0.06	0.08	0.01
	13.90	Herbivore (short grass)	19.60	1.41	14.50	1.04	11.56	0.83	1.18	0.08	6.96	0.50	5.15	0.37	4.11	0.30	0.42	0.03
	13.90	Herbivore (long grass)	11.97	0.86	8.85	0.64	7.06	0.51	0.72	0.05	3.91	0.28	2.89	0.21	2.31	0.17	0.23	0.02
	13.90	Herbivore (forage crops)	18.13	1.30	13.42	0.97	10.70	0.77	1.09	0.08	5.99	0.43	4.44	0.32	3.54	0.25	0.36	0.03

EDE: mg a.i./kg bw

Table 35 Refined Assessment of Reproductive Risk to Mammals (Luna Privilege)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Mammal (0.015 kg)																		
Reproduction	82.4	Insectivore (small insects)	11.71	0.14	8.66	0.11	6.91	0.08	0.70	0.01	6.53	0.08	4.83	0.06	3.85	0.05	0.39	<0.01
	82.4	Granivore (grain and seeds)	2.93	0.04	2.17	0.03	1.73	0.02	0.18	<0.01	1.40	0.02	1.03	0.01	0.82	0.01	0.08	<0.01
	82.4	Frugivore (fruit)	5.85	0.07	4.33	0.05	3.45	0.04	0.35	<0.01	2.79	0.03	2.07	0.03	1.65	0.02	0.17	<0.01
Medium Sized Mammal (0.035 kg)																		
Reproduction	82.4	Insectivore (small insects)	10.26	0.12	7.59	0.09	6.05	0.07	0.62	0.01	5.72	0.07	4.23	0.05	3.38	0.04	0.34	<0.01
	82.4	Insectivore (large insects)	2.57	0.03	1.90	0.02	1.51	0.02	0.15	<0.01	1.22	0.01	0.91	0.01	0.72	0.01	0.07	<0.01
	82.4	Granivore (grain and seeds)	2.57	0.03	1.90	0.02	1.51	0.02	0.15	<0.01	1.22	0.01	0.91	0.01	0.72	0.01	0.07	<0.01
	82.4	Frugivore (fruit)	5.13	0.06	3.80	0.05	3.03	0.04	0.31	<0.01	2.45	0.03	1.81	0.02	1.44	0.02	0.15	<0.01
	82.4	Herbivore (short grass)	36.67	0.45	27.14	0.33	21.64	0.26	2.20	0.03	13.02	0.16	9.64	0.12	7.68	0.09	0.78	0.01
	82.4	Herbivore (long grass)	22.39	0.27	16.57	0.20	13.21	0.16	1.34	0.02	7.31	0.09	5.41	0.07	4.31	0.05	0.44	0.01
	82.4	Herbivore (forage crops)	33.93	0.41	25.11	0.30	20.02	0.24	2.04	0.02	11.22	0.14	8.30	0.10	6.62	0.08	0.67	0.01
Large Sized Mammal (1 kg)																		
Reproduction	82.4	Insectivore (small insects)	5.48	0.07	4.06	0.05	3.24	0.04	0.33	<0.01	3.06	0.04	2.26	0.03	1.80	0.02	0.18	<0.01
	82.4	Insectivore (large insects)	1.37	0.02	1.01	0.01	0.81	0.01	0.08	<0.01	0.65	0.01	0.48	0.01	0.39	<0.01	0.04	<0.01

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
	82.4	Granivore (grain and seeds)	1.37	0.02	1.01	0.01	0.81	0.01	0.08	<0.01	0.65	0.01	0.48	0.01	0.39	<0.01	0.04	<0.01
	82.4	Frugivore (fruit)	2.74	0.03	2.03	0.02	1.62	0.02	0.16	<0.01	1.31	0.02	0.97	0.01	0.77	0.01	0.08	<0.01
	82.4	Herbivore (short grass)	19.60	0.24	14.50	0.18	11.56	0.14	1.18	0.01	6.96	0.08	5.15	0.06	4.11	0.05	0.42	0.01
	82.4	Herbivore (long grass)	11.97	0.15	8.85	0.11	7.06	0.09	0.72	0.01	3.91	0.05	2.89	0.04	2.31	0.03	0.23	<0.01
	82.4	Herbivore (forage crops)	18.13	0.22	13.42	0.16	10.70	0.13	1.09	0.01	5.99	0.07	4.44	0.05	3.54	0.04	0.36	<0.01

EDE: mg a.i./kg bw

Table 36 Screening Level Risk Assessment to Terrestrial Plants (Luna Privilege)

Organism	Exposure	Test Substance	Tox Value for RQ	EEC	RQ
Vascular plants	seedling emergence	Luna Privilege A G	EC_{25}: 500 g a.i./ha	497.76 g a.i./ ha	**1.00**
	vegetative vigour	Luna Privilege A G	EC_{25}: 250 g a.i./ha	403.9 g a.i./ha*	**1.62**

*with a default foliar half-life of 10 days

Table 37 Refined Risk Assessment to Terrestrial Plants (Luna Privilege)

	Airblast Early (74% drift)	Airblast Late (59% drift)	Ground Boom (6% drift)
Application rate (250 g a.i./ha)	185 g a.i./ha	147.5 g a.i./ha	15.00 g a.i/ha
Seedling Emergence			
Cumulative application rate (2 applications, 7 d interval and DT50 of 539 days)	368.34 g a.i./ha	293.68 g a.i./ha	29.87 g a.i./ha
RQ with EC_{25} of 500 g a.i./ha for seedling emergence	0.77	0.59	0.06
Risk	no risk	no risk	no risk
Vegitative vigour			
Cumulative application rate (2 applications, 7 d interval and foliar half-life of 10 days)	298.89 g a.i./ha	238.31 g a.i./ha	24.24 g a.i./ha
RQ with EC_{25} of 250 g a.i./ha for vegitative vogour	1.2	0.95	0.1
Risk	risk	no risk	no risk

Table 38 Screening Level EEC* for Fluopyram (Luna Tranquility Fungicide)

Soil**	Water***	
	15 cm depth	80 cm depth
0.22 mg a.i./kg soil	0.33 mg a.i./L water	0.33 mg a.i./L water

*based on 5 applications of 100 g a.i./ha each with a cumulative application rate 491.12 g
**top 30 cm soil depth and a soil bulk density of 1.5 g/cm^3
*** cumulative application of 496.72 g a.i./ha based on a half-life of 1470 days

Table 39 Maximum EECs Fluopyram in Vegetation and Insects after a Direct Over-Spray (Luna Tranquility Fungicide)

Matrix	EEC[a] (mg a.i./kg fw)	Fresh/Dry Weight Ratios	EEC Direct Overspray (mg a.i./kg dw) Maximum Residues	Mean EEC (mg a.i./kg dw) Mean Residues
Short range grass	50.7537	3.3	167.4873	59.4816
Leaves and leafy crops	28.6966	11	315.6628	104.3513
Long grass	23.2418	4.4	102.2641	33.3924
Forage crops	28.6966	5.4	154.9617	51.2270
Small insects	12.3324	3.8	46.8631	26.1352
Pods with seeds	3.0831	3.9	12.0242	5.7346
Large insects	3.0831	3.8	11.7158	5.5876
Grain and seeds	3.0831	3.8	11.7158	5.5876
Fruit	3.0831	7.6	23.4317	11.1751

[a] Cumulative application rate of 237.162 g a.i./ha (five applications of 100 g a.i. each with 7-day interval and with default half-life of 10 days)

Table 40 Screening Level Risk Assessment to Wild Birds (Luna Tranquility Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	200.00	Insectivore (small insects)	11.95	0.06
Reproduction	4.12	Insectivore (small insects)	11.95	**2.90**
Medium Sized Bird (0.1 kg)				
Acute	200.00	Insectivore (small insects)	9.33	0.05
Reproduction	4.12	Insectivore (small insects)	9.33	**2.26**
Large Sized Bird (1 kg)				
Acute	200.00	Herbivore (short grass)	9.73	0.05
Reproduction	4.12	Herbivore (short grass)	9.73	**2.36**

Table 41 Expanded Screening Level Reproductive Risk Assessment for Wild Birds for On-Field and Off-Field Scenarios (Luna Tranquility Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)																		
Reproduction	4.12	Insectivore (small insects)	11.95	**2.90**	8.84	**2.15**	7.05	**1.71**	0.72	0.17	6.66	**1.62**	4.93	**1.20**	3.93	0.95	0.40	0.10
	4.12	Granivore (grain and seeds)	2.99	0.73	2.21	0.54	1.76	0.43	0.18	0.04	1.42	0.35	1.05	0.26	0.84	0.20	0.09	0.02
	4.12	Frugivore (fruit)	5.98	**1.45**	4.42	**1.07**	3.53	0.86	0.36	0.09	2.85	0.69	2.11	0.51	1.68	0.41	0.17	0.04
Medium Sized Bird (0.1 kg)																		
Reproduction	4.12	Insectivore (small insects)	9.33	**2.26**	6.90	1.68	5.50	**1.34**	0.56	0.14	5.20	**1.26**	3.85	0.93	3.07	0.74	0.31	0.08
	4.12	Insectivore (large insects)	2.33	0.57	1.73	0.42	1.38	0.33	0.14	0.03	1.11	0.27	0.82	0.20	0.66	0.16	0.07	0.02

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
	4.12	Granivore (grain and seeds)	2.33	0.57	1.73	0.42	1.38	0.33	0.14	0.03	1.11	0.27	0.82	0.20	0.66	0.16	0.07	0.02
	4.12	Frugivore (fruit)	4.66	**1.13**	3.45	0.84	2.75	0.67	0.28	0.07	2.22	0.54	1.65	0.40	1.31	0.32	0.13	0.03
Large Sized Bird (1 kg)																		
Reproduction	4.12	Insectivore (small insects)	2.72	0.66	2.01	0.49	1.61	0.39	0.16	0.04	1.52	0.37	1.12	0.27	0.90	0.22	0.09	0.02
	4.12	Insectivore (large insects)	0.68	0.17	0.50	0.12	0.40	0.10	0.04	0.01	0.32	0.08	0.24	0.06	0.19	0.05	0.02	0.00
	4.12	Granivore (grain and seeds)	0.68	0.17	0.50	0.12	0.40	0.10	0.04	0.01	0.32	0.08	0.24	0.06	0.19	0.05	0.02	0.00
	4.12	Frugivore (fruit)	1.36	0.33	1.01	0.24	0.80	0.19	0.08	0.02	0.65	0.16	0.48	0.12	0.38	0.09	0.04	0.01
	4.12	Herbivore (short grass)	9.73	**2.36**	7.20	**1.75**	5.74	**1.39**	0.58	0.14	3.46	0.84	2.56	0.62	2.04	0.49	0.21	0.05
	4.12	Herbivore (long grass)	5.94	**1.44**	4.40	**1.07**	3.51	0.85	0.36	0.09	1.94	0.47	1.44	0.35	1.14	0.28	0.12	0.03
	4.12	Herbivore (forage crops)	9.00	**2.19**	6.66	**1.62**	5.31	**1.29**	0.54	0.13	2.98	0.72	2.20	0.53	1.76	0.43	0.18	0.04

EDE: mg a.i./kg bw

Table 42 Refined Assessment of Reproductive Risk for Wild Birds (Luna Tranquility Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off-field (74%)		Off-field (59%)		Off-field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)																		
Reproduction	6.8	Insectivore (small insects)	11.95	**1.76**	8.84	**1.30**	7.05	**1.04**	0.72	0.11	6.66	0.98	4.93	0.73	3.93	0.58	0.40	0.06
	6.8	Granivore (grain and seeds)	2.99	0.44	2.21	0.33	1.76	0.26	0.18	0.03	1.42	0.21	1.05	0.16	0.84	0.12	0.09	0.01
	6.8	Frugivore (fruit)	5.98	0.88	4.42	0.65	3.53	0.52	0.36	0.05	2.85	0.42	2.11	0.31	1.68	0.25	0.17	0.03
Medium Sized Bird (0.1 kg)																		
Reproduction	6.8	Insectivore (small insects)	9.33	**1.37**	6.90	**1.01**	5.50	0.81	0.56	0.08	5.20	0.76	3.85	0.57	3.07	0.45	0.31	0.05
	6.8	Insectivore (large insects)	2.33	0.34	1.73	0.25	1.38	0.20	0.14	0.02	1.11	0.16	0.82	0.12	0.66	0.10	0.07	0.01
	6.8	Granivore (grain and seeds)	2.33	0.34	1.73	0.25	1.38	0.20	0.14	0.02	1.11	0.16	0.82	0.12	0.66	0.10	0.07	0.01
	6.8	Frugivore (fruit)	4.66	0.69	3.45	0.51	2.75	0.40	0.28	0.04	2.22	0.33	1.65	0.24	1.31	0.19	0.13	0.02
Large Sized Bird (1 kg)																		
Reproduction	6.8	Insectivore (small insects)	2.72	0.40	2.01	0.30	1.61	0.24	0.16	0.02	1.52	0.22	1.12	0.17	0.90	0.13	0.09	0.01
	6.8	Insectivore (large insects)	0.68	0.10	0.50	0.07	0.40	0.06	0.04	0.01	0.32	0.05	0.24	0.04	0.19	0.03	0.02	0.00
	6.8	Granivore (grain and seeds)	0.68	0.10	0.50	0.07	0.40	0.06	0.04	0.01	0.32	0.05	0.24	0.04	0.19	0.03	0.02	0.00
	6.8	Frugivore (fruit)	1.36	0.20	1.01	0.15	0.80	0.12	0.08	0.01	0.65	0.10	0.48	0.07	0.38	0.06	0.04	0.01
	6.8	Herbivore (short grass)	9.73	**1.43**	7.20	1.06	5.74	0.84	0.58	0.09	3.46	0.51	2.56	0.38	2.04	0.30	0.21	0.03
	6.8	Herbivore (long grass)	5.94	0.87	4.40	0.65	3.51	0.52	0.36	0.05	1.94	0.29	1.44	0.21	1.14	0.17	0.12	0.02
	6.8	Herbivore (forage crops)	9.00	**1.32**	6.66	0.98	5.31	0.78	0.54	0.08	2.98	0.44	2.20	0.32	1.76	0.26	0.18	0.03

EDE: mg a.i./kg bw

Table 43 Screening Level Risk Assessment to Mammals (Luna Tranquility Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Mammal (0.015 kg)				
Acute	200.00	Insectivore (small insects)	6.87	0.03
Reproduction	13.90	Insectivore (small insects)	6.87	0.49
Medium Sized Mammal (0.035 kg)				
Acute	200.00	Herbivore (short grass)	21.53	0.11
Reproduction	13.90	Herbivore (short grass)	21.53	**1.55**
Large Sized Mammal (1 kg)				
Acute	200.00	Herbivore (short grass)	11.51	0.06
Reproduction	13.90	Herbivore (short grass)	11.51	0.83

Table 44 Expanded Screening Level Reproductive Risk Assessment for Mammals (Luna Tranquility Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Medium Mammal (0.055 kg)																		
Reproduction	13.90	Insectivore (small insects)	6.03	0.43	4.46	0.32	3.55	0.26	0.36	0.03	3.36	0.24	2.49	0.18	1.98	0.14	0.20	0.01
	13.90	Insectivore (large insects)	1.51	0.11	1.11	0.08	0.89	0.06	0.09	0.01	0.72	0.05	0.53	0.04	0.42	0.03	0.04	0.00
	13.90	Granivore (grain and seeds)	1.51	0.11	1.11	0.08	0.89	0.06	0.09	0.01	0.72	0.05	0.53	0.04	0.42	0.03	0.04	0.00
	13.90	Frugivore (fruit)	3.01	0.22	2.23	0.16	1.78	0.13	0.18	0.01	1.44	0.10	1.06	0.08	0.85	0.06	0.09	0.01
	13.90	Herbivore (short grass)	21.53	**1.55**	15.94	**1.15**	12.71	0.91	1.29	0.09	7.65	0.55	5.66	0.41	4.51	0.32	0.46	0.03
	13.90	Herbivore (long grass)	13.15	0.95	9.73	0.70	7.76	0.56	0.79	0.06	4.29	0.31	3.18	0.23	2.53	0.18	0.26	0.02
	13.90	Herbivore (forage crops)	19.92	**1.43**	14.74	**1.06**	11.75	0.85	1.20	0.09	6.59	0.47	4.87	0.35	3.89	0.28	0.40	0.03

EDE: mg a.i./kg bw

Table 45 Refined Assessment of Reproductive Risk for Mammals (Luna Tranquility Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Food Guild (food item)	Maximum Residues								Mean Residues							
			On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)		On-field		Off Field (74%)		Off Field (59%)		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Medium sized Mammal (0.035 kg)																		
Reproduction	82.4	Insectivore (small insects)	6.03	0.07	4.46	0.05	3.55	0.04	0.36	0.00	3.36	0.04	2.49	0.03	0.04	1.98	0.20	0.00
	82.4	Insectivore (large insects)	1.51	0.02	1.11	0.01	0.89	0.01	0.09	0.00	0.72	0.01	0.53	0.01	0.01	0.42	0.04	0.00
	82.4	Granivore (grain and seeds)	1.51	0.02	1.11	0.01	0.89	0.01	0.09	0.00	0.72	0.01	0.53	0.01	0.01	0.42	0.04	0.00
	82.4	Frugivore (fruit)	3.01	0.04	2.23	0.03	1.78	0.02	0.18	0.00	1.44	0.02	1.06	0.01	0.02	0.85	0.09	0.00
	82.4	Herbivore (short grass)	21.53	0.26	15.94	0.19	12.71	0.15	1.29	0.02	7.65	0.09	5.66	0.07	0.09	4.51	0.46	0.01
	82.4	Herbivore (long grass)	13.15	0.16	9.73	0.12	7.76	0.09	0.79	0.01	4.29	0.05	3.18	0.04	0.05	2.53	0.26	0.00
	82.4	Herbivore (forage crops)	19.92	0.24	14.74	0.18	11.75	0.14	1.20	0.01	6.59	0.08	4.87	0.06	0.08	3.89	0.40	0.00

EDE: mg a.i./kg bw

Table 46 Screening Level Risk Assessment to Terrestrial Plants (Luna Tranquility Fungicide)

Organism	Exposure	Test Substance	Tox Value For RQ	EEC	RQ
Vascular plants	seedling emergence	AE C656948 SC 500A G	EC_{25}: 500 g a.i./ha	491.12 g a.i./ ha*	0.98
	vegetative vigour	AE C656948 SC 500A G	EC_{25}: 250 g a.i./ha	237.162 g a.i./ha	0.95

*based the cumulative rate with a field DT50 of 539 days; ** with a default foliar half-life of 10 days

Table 47 Screening Level Risk Assessment to Wild Birds (Propulse Fungicide)

Effects	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	EDE (mg a.i./kg bw)	RQ
Small Bird (0.02 kg)				
Acute	200.00	Insectivore (small insects)	12.21	0.06
Reproduction	4.12	Insectivore (small insects)	12.21	**2.96**
Medium Sized Bird (0.1 kg)				
Acute	200.00	Insectivore (small insects)	9.53	0.05
Reproduction	4.12	Insectivore (small insects)	9.53	**2.31**
Large Sized Bird (1 kg)				
Acute	200.00	Herbivore (short grass)	9.94	0.05
Reproduction	4.12	Herbivore (short grass)	9.94	**2.41**

Table 48 Expanded Screening Level Reproductive Risk Assessment for Wild Birds (Propulse Fungicide)

Effects	Toxicity mg a.i./kg bw/d	Food Guild (food item)	Maximum residues				Mean residues			
			On-field		Off-field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)										
Reproduction	4.12	Insectivore (small insects)	12.21	**2.96**	0.73	0.18	6.81	**1.65**	0.41	0.10
	4.12	Granivore (grain and seeds)	3.05	0.74	0.18	0.04	1.46	0.35	0.09	0.02
	4.12	Frugivore (fruit)	6.11	**1.48**	0.37	0.09	2.91	0.71	0.17	0.04
Medium Sized Bird (0.1 kg)										
Reproduction	4.12	Insectivore (small insects)	9.53	**2.31**	0.57	0.14	5.31	**1.29**	0.32	0.08
	4.12	Insectivore (large insects)	2.38	0.58	0.14	0.03	1.14	0.28	0.07	0.02
	4.12	Granivore (grain and seeds)	2.38	0.58	0.14	0.03	1.14	0.28	0.07	0.02
	4.12	Frugivore (fruit)	4.76	**1.16**	0.29	0.07	2.27	0.55	0.14	0.03

Effects	Toxicity mg a.i./kg bw/d	Food Guild (food item)	Maximum residues				Mean residues			
			On-field		Off-field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Large Sized Bird (1 kg)										
Reproduction	4.12	Insectivore (small insects)	2.78	0.68	0.17	0.04	1.55	0.38	0.09	0.02
	4.12	Insectivore (large insects)	0.70	0.17	0.04	0.01	0.33	0.08	0.02	0.00
	4.12	Granivore (grain and seeds)	0.70	0.17	0.04	0.01	0.33	0.08	0.02	0.00
	4.12	Frugivore (fruit)	1.39	0.34	0.08	0.02	0.66	0.16	0.04	0.01
	4.12	Herbivore (short grass)	9.94	**2.41**	0.60	0.14	3.53	0.86	0.21	0.05
	4.12	Herbivore (long grass)	6.07	**1.47**	0.36	0.09	1.98	0.48	0.12	0.03
	4.12	Herbivore (forage crops)	9.20	**2.23**	0.55	0.13	3.04	0.74	0.18	0.04

EDE: mg a.i./kg bw

Table 49 Refined Reproductive Risk Assessment for Wild Birds (Propulse Fungicide)

Effects	Toxicity	Food Guild (food item)	Maximum residues				Mean residues			
			On-field		Off-field (6%)		On-field		Off Field (6%)	
			EDE	RQ	EDE	RQ	EDE	RQ	EDE	RQ
Small Bird (0.02 kg)										
Reproduction	6.8	Insectivore (small insects)	12.21	**1.80**	0.73	0.11	6.81	**1.00**	0.41	0.06
	6.8	Granivore (grain and seeds)	3.05	0.45	0.18	0.03	1.46	0.21	0.09	0.01
	6.8	Frugivore (fruit)	6.11	0.90	0.37	0.05	2.91	0.43	0.17	0.03
Medium Sized Bird (0.1 kg)										
Reproduction	6.8	Insectivore (small insects)	9.53	**1.40**	0.57	0.08	5.31	0.78	0.32	0.05
	6.8	Insectivore (large insects)	2.38	0.35	0.14	0.02	1.14	0.17	0.07	0.01
	6.8	Granivore (grain and seeds)	2.38	0.35	0.14	0.02	1.14	0.17	0.07	0.01
	6.8	Frugivore (fruit)	4.76	0.70	0.29	0.04	2.27	0.33	0.14	0.02
Large Sized Bird (1 kg)										
Reproduction	6.8	Insectivore (small insects)	2.78	0.41	0.17	0.02	1.55	0.23	0.09	0.01
	6.8	Insectivore (large insects)	0.70	0.10	0.04	0.01	0.33	0.05	0.02	0.00
	6.8	Granivore (grain and seeds)	0.70	0.10	0.04	0.01	0.33	0.05	0.02	0.00
	6.8	Frugivore (fruit)	1.39	0.20	0.08	0.01	0.66	0.10	0.04	0.01
	6.8	Herbivore (short grass)	9.94	**1.46**	0.60	0.09	3.53	0.52	0.21	0.03
	6.8	Herbivore (long grass)	6.07	0.89	0.36	0.05	1.98	0.29	0.12	0.02
	6.8	Herbivore (forage crops)	9.20	**1.35**	0.55	0.08	3.04	0.45	0.18	0.03

EDE: mg a.i./kg bw

Table 50 Screening Level Risk Assessment to Terrestrial Plants (Propulse Fungicide)

Organism	Exposure	Test Substance	Tox Value For RQ	EEC	RQ
Vascular plants	seedling emergence	AE C656948 SC 500A G	EC25: 500.00 g a.i./ha	298.656 g a.i./ ha	**0.60**
	vegetative vigour	AE C656948 SC 500A G	EC_{25}:250.00g a.i./ha	242.345 g a.i./ha	**0.97**

Table 51 Effects on Aquatic Organisms

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity	PMRA #
Freshwater species					
Rainbow trout (*Oncorhynchus mykiss)*	acute (96 h)	AE C656948	LC_{50}: >1.78 mg a.i./L NOAEC: 1.78 mg a.i./L	moderately toxic	1599539
	acute (96 h)	Luna Privilege G	LC_{50}: >46.4 mg a.i./L NOAEC: 1.31 mg a.i./L EC_{50}: 3.71 mg a.i./L (sub-lethal effects)	slightly toxic	1599284
Bluegill sunfish *(Lepomis macrochirus*)	acute (96 h)	AE C656948	LC_{50}: >5.17 mg a.i./L NOAEC: 5.17 mg a.i./L	moderately toxic	1599538
Fathead minnow (*Pimephales promelas*)	acute (96 h)	AE C656948	LC_{50}: >4.95 mg a.i./L NOAEC: 4.95 mg a.i./L EC_{50}: >4.95 mg a.i./L	moderately toxic	1599543
Fathead minnow (*Pimephales promelas*)	chronic: early life stage (33 d)	AE C656948	NOAEC: 0.135 mg a.i./L LOAEC: 0.269 mg a.i./L	N/A	1599730
Daphnia *(Daphnia magna)*	acute (48 h)	AE C656948	NOAEC: 17 mg a.i./L EC_{50}: >17 mg a.i./L	slightly toxic	1599541
	chronic (Life cycle: 21 d)	AE C656948	NOAEC: 1.214 mg a.i./L LOAEC: 2.996 mg a.i./L 21-d EC_{50}: 2.700 mg a.i./L (reproduction)	N/A	1599770
	acute (48 h)	Luna Privilege G	48-h EC_{50}: >38.2 mg a.i./L NOAEC: 11.6 mg a.i./L	slightly toxic	1599285
Freshwater green algae (*Pseudokirchneriella subcapitata)*	acute (96 h)	AE C656948	NOAEC: 1.46 mg a.i./L EC_{50}: 4.3 mg a.i./L (Biomass)	N/A	1599864
	acute (72 h)	Luna Privilege G	NOAEC: 1.17 mg a.i./L EC_{05}: 1.0 mg a.i./L EC_{50}: 3.4 mg a.i./L (Cell density)	N/A	1599287
	acute (72 h)	Fluopyram-Lactame (a metabolite of Fluopyram)	NOAEC: 8.87 mg a.i./L EC_{50}: >8.87 mg a.i./L (growth inhibition)	N/A	1599808
Freshwater diatom *(Navicula pelliculosa)*	acute (96 h)	AE C656948	NOAEC: 2.47 mg a.i./L EC_{50}: 6.1 mg a.i./L (biomass)	N/A	1599862
Freshwater blue-green algae *(Anabaena flos-aquae)*	acute (96 h)	AE C656948	NOAEC: 9.69 mg a.i./L EC_{50}: >9.69 mg a.i./L most sensitive end-point: none	N/A	1599863
Duckweed (*Lemna gibba*)	acute (7 d)	AE C656948	NOAEC: 0.278 mg a.i./L EC_{05} > 0.278 mg a.i./L EC_{50}: 2.6 mg a.i./L (frond number based on yield)	N/A	1599773
	acute (7 d)	Luna Privilege G	NOAEC: 1.04 mg a.i./L EC_{05}: 1.8 mg a.i./L EC_{50}: 2.9 mg a.i./L (frond number)	N/A	1599303
Sediment dwelling Freshwater chironomid (*Chironomus riparius)*	28-d chronic	AE C656948	overlying water concentrations* EC_{50} (emergence ratio): >5.52 mg a.i./L NOAEC (emergence ratio): >0.0128 and <3.11 mg a.i./L	N/A	1599633

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity	PMRA #
			0.525 mg a.i./L (TWA)		
Freshwater dipteran midge (*Chironomus tentans)*	54-day life-cycle	AE C656948	NOAEC (survival and emergences): sediment: 26 mg a.i./kg pore water: 3.8 mg a.i./L (TWA) overlying water: 0.14 mg a.i./L	N/A	1599614
Marine species					
Sheepshead Minnow (*Cyprinodon variegatus*)	acute (96 h)	AE C656948	LC_{50}: >0.98 mg a.i./L NOAEC: 0.98 mg a.i./L EC_{50}: >0.98 mg a.i./L	highly toxic	1599544
Eastern Oyster (*Crassostrea virginica)*	acute (96 h)	AE C656948	EC_{50}: >0.43 mg a.i./L NOAEC: 0.43 mg a.i./L (shell deposition)	highly toxic	1599604
Saltwater Mysid (*Americamysis bahia*)	acute (96 h)	AE C656948	LC_{50}: >0.51 mg a.i./L NOAEC: 0.27 mg a.i./L	highly toxic	1599603
Saltwater Diatom *(Skeletonema costatum)*	acute (96 h)	AE C656948	EC_{50}: > 1.13 mg a.i./L NOAEC: 1.13 mg a.i./L (cell density, biomass, growth rate) most sensitive end-point: none	moderately toxic	1599865
Marine amphipods (*Leptocheirus plumulosus*)	10-d acute	AE C656948	<u>sediment concentrations</u> LC_{50} mortality: >100 mg a.i./kg NOAEC (mortality): 100 mg a.i./kg <u>Pore water concentrations</u> LC_{50} mortality: >7.5 mg a.i./L NOAEC (mortality): 7.5 mg a.i./L <u>Overlying water concentrations</u> LC_{50} mortality: >1.6 mg a.i./L NOAEC (mortality): 1.6 mg a.i./L	moderately toxic	1599616
Marine amphipods (*Leptocheirus plumulosus*)	28-d chronic	AE C656948	<u>sediment concentrations</u> (Total radioactive residues equivalent to a.i) EC_{50} growth: >92 mg a.i./kg NOAEC (growth): 36 mg a.i./kg <u>pore water concentrations</u> EC_{50} growth: >5.9 mg a.i./L NOAEC (growth): 2.5 mg a.i./L <u>overlying water concentrations</u> EC_{50} growth: >1.19 mg a.i./L NOAEC (growth): 0.55 mg a.i./L	N/A	1599615

*sediment concentrations not measured; **TWA Time weighted average

Table 52 Screening Level Risk Assessment to Aquatic Organisms (Luna Privilege)

Organism	Exposure	Test Substance	Tox Value For RQ (mg a.i./L)	EEC (mg a.i./L)	RQ
Rainbow trout (*O. mykiss)*	acute	AEC 656948	(LC_{50}/10): >0.178**	0.062*	<0.35
Bluegill sunfish *(L. macrochirus*)	bioaccumulation study	AE C656948	BCF: 18	low potential for bioaccumulation	
Fathead minnow (*P. promelas*)	chronic: early life stage	AE C656948	NOAEC: 0.135	0.062*	0.46
Sediment dwelling *(C. riparius)* *(C. tetans)*	54 d pore water	AE C656948	NOAEC: 3.8	0.062*	0.16
	54 d sediment	AE C656948	NOAEC: 26	0.062*	0.002
Amphibians	acute	AE C656948	(LC_{50}/10): >0.178**	0.33£	**<1.85**
	chronic	AE C656948	NOAEC: 0.135	0.33£	**2.44**
Daphnia *(D. magna)*	Acute	AE C656948	(EC_{50}/2): >8.5***	0.062*	<0.017
	chronic	AE C656948	NOAEC: 1.214	0.062*	0.05
Freshwater green algae (*P. subcapitata)*	acute	Luna Privilege G	(EC_{50}/2):1.7***	0.062*	0.04
Freshwater diatom *(N. pelliculosa)*	acute	AE C656948	(EC_{50}/2): 3.1***	0.062	0.02
Duckweed (*L. gibba*)	acute	AE C656948	(EC_{50}/2): 1.3***	0.062*	0.05
Sheepshead Minnow (*C. variegatus*)	acute	AE C656948	(LC_{50}/10): >0.098**	0.062*	<0.63
Eastern Oyster (*C. virginica)*	acute	AE C656948	(LC_{50}/2): 0.22***	0.062*	0.28
Saltwater Diatom *(S. costatum)*	acute	AE C656948	(EC_{50}/2): >0.57***	0.062*	<0.11
Marine amphipods (*Leptocheirus plumulosus*)	acute	AE C656948	(LC_{50}/2): >0.8*** (overlying water)	0.062*	<0.08
	chronic	AE C656948	NOAEC: 0.55 (overlying water)	0.062*	0.11

* 80 cm water depth; £15 cm water depth
** with an uncertainty factor of 10
*** with an uncertainty factor of 2

Table 53 Refined Risk Assessment to Amphibians: Run off (Luna Privilege)

	Exposure	Test Substance	Tox Value For RQ (mg a.i./L)	EEC (mg a.i./L)	RQ
Run off	acute	AE C656948	(LC_{50}/10): >0.178	0.299*	**<1.68**
	chronic	AE C656948	NOAEC: 0.135	0.261**	**1.93**

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

Table 54 Refined Risk Assessment to Amphibians: Spray Drift (Luna Privilege)

	Airblast early (74% drift)	Airblast late (59% drift)	Ground boom (6% drift)
Application rate (250 g a.i./ha)	185 g a.i./ha	147.5 g a.i./ha	15.00 g a.i/ha
Cumulative application rate (2 applications, 7 d interval)	369.39 g a.i./ha	294.51 g a.i./ha	29.95 g a.i./ha
EEC	0.25 mg a.i./L	0.20 mg a.i./L	0.02mg a.i./L
Acute RQ(LC_{50}: 0.178 mg a.i./L)	**1.40**	**1.12**	0.11
Chronic RQ (NOEC: 0.135 mg a.i./L)	**1.85**	**1.48**	0.15
Risk	yes	yes	no

Table 55 Screening Level and Refined Risk Assessment to Amphibians: Spray Drift from Aerial Application (Potato)

	Screening level (direct overspray)	Aerial application-in off-field (23% drift)
Application rate (400 g a.i./ha)	398.5 g a.i./ha (cumulative)	91.7 g a.i./ha
EEC in 15 cm water depth	0.266 mg a.i./L	0.061 mg a.i./L
Acute RQ(LC_{50}: 0.178 mg a.i./L)	**1.49**	0.34
Chronic RQ (NOEC: 0.135 mg a.i./L)	**1.97**	0.45
Risk	yes	no

Table 56 Screening Level Risk Assessment to Amphibians (Propulse Fungicide)

Exposure	Test Substance	Tox Value for RQ (mg a.i./L)	EEC (mg a.i./L)	RQ
Acute	AE C656948	(LC_{50}/10): 0.178	0.2*	**1.12**
Chronic	AE C656948	NOAEC: 0.135	0.2*	**1.48**

* 15 cm water depth

Table 57 Refined Risk Assessment to Amphibians: Run Off (Propulse Fungicide)

Exposure	Test Substance	Tox Value For RQ (mg a.i./L)	EEC (mg a.i./L)	RQ
Acute	AE C656948	(LC_{50}/10): >0.178	0.179*	**<1.00**
Chronic	AE C656948	NOAEC: 0.135	0.157**	**1.16**

** 15 cm water depth and 21-day EEC

Table 58 Refined Risk Assessment to Amphibians: Spray Drift (Propulse Fungicide)

Use Pattern	Ground Boom (6% drift)
Application rate (150 g a.i./ha)	9.00 g a.i/ha
Cumulative application rate (2 applications, 7 d interval)	17.97 g a.i./ha
EEC	0.002mg a.i./L
Acute RQ(LC_{50}:0.178 mg a.i./L)	0.01
Chronic RQ (NOEC:0.135 mg a.i./L)	0.01
Risk	no

Table 59 Luna Privilege Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed use claim	Supported Use
To control powdery mildew on watermelon, apply Luna Privilege at a rate of 150-250 mL/ha at seven to fourteen day intervals.	Supported as proposed
To control botrytis grey mold on watermelon, apply Luna Privilege at a rate of 500 mL/ha at seven to ten day intervals.	Supported as proposed
To control botrytis bunch rot / grey mold on wine grape, apply Luna Privilege at a rate of 500 mL/ha at early bloom and at berry touch to bunch closure.	Supported as proposed
To control white mold on dry bean, apply Luna Privilege at a rate of 300 mL/ha at seven to fourteen day intervals.	Supported as proposed
To control ascochyta blight on dry bean, apply Luna Privilege at a rate of 300 mL/ha at ten to fourteen day intervals.	Supported as proposed
To control mycosphaerella blight on dry bean, apply Luna Privilege at a rate of 300 mL/ha at ten to fourteen day intervals.	Supported as proposed
To control powdery mildew on dry bean, apply Luna Privilege at a rate of 150-250 mL/ha at seven to fourteen day intervals.	Supported as proposed
To control early leaf spot on peanut, apply Luna Privilege at a rate of 250-500 mL/ha at a 14 day intervals.	Supported as proposed
To control late leaf spot on peanut, apply Luna Privilege at a rate of 250-500 mL/ha at a 14 day intervals.	Supported as proposed
To control leaf scab on apple, apply Luna Privilege at a rate of 300 mL/ha at seven to fourteen day intervals.	Supported as proposed
To control early blight on potato, apply Luna Privilege at a rate of 150-300 mL/ha at seven to twelve day intervals.	Supported as proposed
To control powdery mildew on strawberry, apply Luna Privilege at a rate of 500 mL/ha through drip irrigation at five to seven day intervals.	Supported as proposed
To control brown rot blossom blight on sweet and tart cherry, apply Luna Privilege at a rate of 250 mL/ha at fourteen day intervals.	Supported as proposed but limited to three seasonal applications rather than four for resistance management considerations
To control powdery mildew on sweet and tart cherry, apply Luna Privilege at a rate of 150-250 mL/ha at seven to fourteen day intervals.	Supported as proposed but limited to three seasonal applications rather than four for resistance management considerations
To control brown rot blossom blight on tree nuts, apply Luna Privilege at a rate of 250-500 mL/ha at fourteen day intervals.	Supported as proposed on almonds, the only susceptible tree nut in the crop group.

Table 60 Luna Tranquility Fungicide Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed use claim	Supported Use
To control powdery mildew on wine grape, apply Luna Tranquility Fungicide at a rate of 600 mL/ha at seven to fourteen day intervals.	Supported as proposed with a limit of four applications per season instead of six.
To control botrytis bunch rot / grey mold on wine grape, Luna Tranquility Fungicide at a rate of 1200 mL/ha at early bloom and at berry touch to bunch closure.	Supported as proposed
To control powdery mildew on apple, apply Luna Tranquility Fungicide at a rate of 600 mL/ha at seven to fourteen day intervals.	Supported as proposed with a limit of four applications per season instead of six.
To control leaf scab on apple, apply Luna Tranquility Fungicide at a rate of 800 mL/ha at seven to fourteen day intervals.	Supported as proposed with a limit of four applications per season instead of six.

Table 61 Propulse Fungicide Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Proposed use claim	Supported Use
To control white mold on dry bean, apply Propulse Fungicide at a rate of 750 mL/ha at seven to fourteen day intervals.	Supported as proposed
To control ascochyta blight on dry bean, apply Propulse Fungicide at a rate of 500-750 mL/ha at ten to fourteen day intervals.	Supported as proposed
To control mycosphaerella blight on dry bean, apply Propulse Fungicide at a rate of 500-750 mL/ha at ten to fourteen day intervals.	Supported as proposed

Table 62 Active Ingredients Currently Registered for Management of Crop Diseases on the Luna Privilege Fungicide, Luna Tranquility Fungicide, and Propulse Fungicide Labels

Crops	Diseases	Active Ingredients (Resistance Management Group)
Watermelon	Powdery mildew[1]	*Bacillus subtilis* QST 713 (44)
		chlorothalonil (M5)
		difenoconazole (3)
		folpet (M4)
		potassium bicarbonate (NC)
		pyraclostrobin (22)
		Streptomyces lydicus WYEC 108 (NC)
	Botrytis grey mold[1]	ferbam (M3)
		Gliocladium catenulatum J1446 (NC)
		iprodione (2)

Crops	Diseases	Active Ingredients (Resistance Management Group)
Wine Grape	Botrytis bunch rot / Grey mold[1,3]	*Bacillus subitlis* QST 713 (44)
		boscalid (7) + pyraclostrobin (11)
		fenhexamid (17)
	Powdery mildew[3]	*Bacillus subtilis* QST 713 (44)
		boscalid (7)
		calcium polysulfide (M2)
		copper oxychloride (M2)
		difenoconazole (3)
		folpet (M4)
		kresoxim-methyl (11)
		metrafenone (U8)
		myclobutanil (3)
		potassium bicarbonate (NC)
		pyraclostrobin (11) + boscalid (7)
		quinoxyfen (13)
		sulphur (M2)
		trifloxystrobin (11)
Dry Bean (Including Chickpea and Lentil)	White mold[1,2]	*Bacillus subtilis* QST 713 (44)
		boscalid (7)
		Coniothyrium minitans CON/M/91-08 (NC)
		cyprodinil (9) + fludioxonil (12)
		dicloran (14)
		fluazinam (29)
		iprodione (2)
		vinclozolin (2)
	Ascochyta blight[1,2]	azoxystrobin (11)
		pyraclostrobin (11)
	Mycosphaerella blight[1,2]	azoxystrobin (11)
		pyraclostrobin (11)
	Powdery mildew[1]	azoxystrobin (11) + propiconazole (3)
		propiconazole (3)
		pyraclostrobin (11)
Peanut	Early Leaf Spot[1]	*Bacillus subtilis* QST 713 (44)
		prothioconazole (3)
	Late Leaf Spot[1]	*Bacillus subtilis* QST 713 (44)
Apple	Leaf scab[1,3]	*Bacillus subtilis* QST 713 (44)
		boscalid (7) + pyraclostrogbin (11)
		calcium polysulphide (M2)
		captan (M4)
		cyprodinil (9)
		difenoconazole (3)
		dodine (M7)
		ferbam (M3)
		fluazinam (29)

Crops	Diseases	Active Ingredients (Resistance Management Group)
		flusilazole (3)
		folpet (M4)
		kresoxim-methyl (11)
		mancozeb (M3)
		mancozeb (M3) + myclobutanil (3)
		metiram (M2)
		myclobutanil (3)
		pyrimethanil (9)
		penthiopyrad (7)
		sulphur (M2)
		thiophanate-methyl (1)
		thiram (M3)
		trifloxystrobin (11)
		ziram (M3)
	Powdery mildew[3]	*Bacillus subtilis* QST 713 (44)
		boscalid (7) + pyraclostrogbin (11)
		calcium polysulphide (M2)
		chlorothalonil (M5)
		cyprodinil (9)
		difenoconazole (3)
		flusilazole (3)
		kresoxim-methyl (11)
		myclobutanil (3)
		sulphur (M2)
		thiophanate-methyl (1)
		trifloxystrobin (11)
Potato	Early blight[1]	azoxystrobin (11)
		Bacillus subtilis QST 713 (44)
		boscalid (7)
		captan (M4)
		chlorothalonil (M5)
		copper – different salts (M1)
		difenoconazole (3)
		dimethomorph (40) + mancozeb (M3)
		famoxadone (11) + cymoxanil (27)
		mancozeb (M3)
		mancozeb (M3) + zoxamide (22)
		maneb (M3)
		metalaxyl (4) + chlorothalonil (M5)
		metalaxyl (4) + mancozeb (M3)
		metiram (M3)
		pyraclostrobin (11)
		zineb (M3)
		zoxamide (22)

Crops	Diseases	Active Ingredients (Resistance Management Group)
Strawberry	Powdery mildew[1]	boscalid (7) + pyraclostrobin (11)
		calcium polysulphide (M2)
		citric acid (NC) + lactic acid (NC)
		myclobutanil (3)
		quinoxyfen (13)
		Streptomyces lydicus WYEC 108 (NC)
Cherry	Brown rot blossom blight[1]	*Bacillus subtilis* QST 713 (44)
		boscalid (7)
		boscalid (7) + pyraclostrobin (11)
		chlorothalonil (M5)
		cyprodinil (9)
		dicloran (14)
		fenhexamid (17)
		pyraclostrobin (11)
	Powdery mildew[1]	boscalid (7) + pyraclostrobin (11)
		quinoxyfen (13)
Almond	Brown rot / blossom blight[1]	chlorothalonil[4] (M5)

[1]claim appears on the Luna Privilege label
[2]claim appears on the Propulse Fungicide label
[3]claim appears on the Luna Tranquility Fungicide label
[4] registered for ornamental applications only

Table 63 TSMP 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		
Predominantly anthropogenic[2]	yes		
Persistence[3]:	soil	half-life: ≥ 182 days	field DT_{50}: 539 days
	water	half-life: ≥ 182 days	half-life: 1470 days (water+sediment)
	sediment	half-life: ≥ 365 days	not available
	air	half-life ≥ 2 days or evidence of long range transport	1.7 to 2.6 days
Bioaccumulation[4]	log K_{OW} ≥ 5		3.3
	BCF ≥ 5000		18
	BAF ≥ 5000		
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 (that is, 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 (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, logK_{ow}).

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

Fluopyram is a new active ingredient, which is concurrently being registered in the United States. American tolerances (40 CFR Part 180) and Codex MRLs established for fluopyram differ from the Canadian maximum residue limits (MRLs) as shown in table below.

Table 1 Differences Between MRLs in Canada and in Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Wine grapes	2.0	2.0	2 (Grapes); 5 (Dried grapes)
Canola	1.8	1.8	Not reviewed by Codex
Crop Group 15 (except rice) – Cereal Grains, except rice; Strawberries	1.5	1.5	
Cherries	1.5	0.6	
Bananas; Watermelon	1.0	1.0	
Dry chickpeas and dry lentils	0.4	None	
Apples	0.3	0.3	
Sugar beet roots	0.1	0.04	
Dry soybeans	0.1	0.1	
Grain lupin, dry kidney beans, dry lima beans, dry navy beans, dry pink beans, dry pinto beans, dry tepary beans, dry beans, dry adzuki beans, dry blackeyed peas, dry catjang seed, dry cowpea seed, dry moth beans, dry mung beans, dry rice beans, dry southern peas, dry urd beans, dry broad beans, dry guar seed, dry lablab beans	0.09	0.09	
Crop Group 14 – Tree Nuts Group	0.05	0.05	
Crop Subgroup 1C – Tuberous and Corm Vegetables Subgroup	0.02	0.02 (potato)	
Peanuts	0.02	0.02	
Undelinted cotton seeds	0.01	0.01	
Eggs	0.06	0.25	
Meat byproducts of poultry	0.10	0.60	
Fat of poultry	0.03	0.20	
Meat of poultry	0.03	0.15	
Milk	0.06	0.07	0.07
Meat byproducts of cattle, goats, horses and sheep	0.40	1.1	0.7 (Edible offal, mammalian); 0.1 (Meat from mammals other than marine mammals)
Fat of cattle, goats, horses and sheep	0.05	0.11	
Meat of cattle, goats, horses and sheep	0.05	0.15	
Meat byproducts of hogs	0.03	0.70	
Fat and meat of hogs	0.02	0.05	

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

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

Under the North American Free Trade Agreement 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

A. List of Studies/Information Submitted by Registrant

1. Chemistry

PMRA Document Number	Reference
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1599499	2008, 1st amendment to report no. 20070286.01 - Fluopyram, AE C656948 - Melting point A.1. (OECD 102), Boiling point A.2. (OECD 103), Thermal stability (OECD 113), DACO: 2.14.13,2.14.4,2.14.5,IIA 2.1.1,IIA 2.1.2,IIA 2.1.3
1599500	2008, 1st amendment to report no. 20070286.03 - Fluopyram, AE C656948 - Explosive properties A.14., DACO: 2.16,IIA 2.13
1599502	2008, 1st amendment to report no. 20070359.01 - Fluopyram, AE C656948, pure substance - Product code: AE C656948 001B99 0001 - Melting point A.1. (OECD 102), Boiling point A.2. (OECD 103), Thermal stability (OECD 113), DACO: 2.14.13,2.14.4,2.14.5,IIA
1599504	2008, 1st amendment to storage stability of AE C656948, DACO: 2.14.14,IIA 2.17.1
1599549	2008, AE C656948 Determination of active substance in technical material HPLC - internal standard, DACO: 2.13.1,IIA 4.2.1
1599565	2008, AE C656948 - By-products in technical grade active substance [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI
1599628	2008, Analytical procedure for the Karl Fischer water determination, DACO: 2.13.4,IIA 4.2.3 CBI
1599637	2007, Composition statement - Technical grade active substance - Fluopyram - Fluopyram TC, AE C656948, DACO: 2.12.2,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9,IIA 1.10.1 CBI
1599641	2008, Determination of [CBI removed] in technical grade active substance [C BI removed], DACO: 2.13.4,IIA 4.2.3 CBI
1599643	2008, Determination of the pH-value of AE C656948 pure substance, DACO: 2.16,IIA 2.16
1599675	2008, Determination of the storage stability of AE C656948 and its metabolites [CBI removed] in soil - results for an interval of 0 to 323 days, DACO: 2
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1599678	2008, Dissociation constant of fluopyram (AE C656948) in water, DACO: 2.14.10,8.2.3.2,IIA 2.9.5
1599742	2008, Fluopyram (AE C656948) - Statement on the ecotoxicological assessment of the proposed technical specification, DACO: 2.13.3,IIA 1.11.2 CBI
1599743	2008, Fluopyram (AE C656948) - Toxicological equivalence assessment of the technical specification with the material tested in toxicity studies, DACO: 2.13.3,IIA 1.11.2 CBI

1599744 2008, Fluopyram (AE C656948): Statement on the dielectric breakdown voltage according to OPPTS 830.6321, DACO: 2.16,IIA 2.18
1599745 2008, Fluopyram (AE C656948): Statement on the miscibility according to OPPTS 830.6319, DACO: 2.16,IIA 2.18
1599746 2008, Fluopyram (AE C656948): Statement on the pH independence of the partition coefficient 1-octanol / water, DACO: 2.14.11,IIA 2.8.2
1599747 2008, Fluopyram (AE C656948): Statement on the viscosity according to OPPTS 830.7100, DACO: 2.16,IIA 2.18
1599748 2008, Fluopyram (AEC 656948) - Technical grade active substance - Discussion of the formation of impurities, DACO: 2.11.1,2.11.3,2.11.4,2.12.2,IIA 1.10.1,IIA 1.8.1 CBI
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1599756 2008, Fluopyram, AE C656948 - Auto-flammability (solids - determination of relative self-ignition temperature) A.16., DACO: 2.16,IIA 2.11.2
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1599776 2008, Material accountability chronic tox sample of fluopyram, DACO: 2.13.3,IIA 1.11.2 CBI
1599777 2008, Material accountability of Fluopyram batches used in toxicological and ecotoxicological studies, DACO: 2.13.3,IIA 1.11.2 CBI
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2.0 Human and Animal Health

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4.0 Value

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