



Health  
Canada

Santé  
Canada

*Your health and  
safety... our priority.*

*Votre santé et votre  
sécurité... notre priorité.*

Evaluation Report

ERC2014-02

# Fluopyram

*(publié aussi en français)*

**22 August 2014**

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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](mailto:pmra.publications@hc-sc.gc.ca)  
[healthcanada.gc.ca/pmra](http://healthcanada.gc.ca/pmra)  
Facsimile: 613-736-3758  
Information Service:  
1-800-267-6315 or 613-736-3799  
[pmra.infoserv@hc-sc.gc.ca](mailto:pmra.infoserv@hc-sc.gc.ca)

Canada 

ISSN: 1925-1238 (print)  
1911-8082 (online)

Catalogue number: H113-26/2014-2E (print version)  
H113-26/2014-2E-PDF (PDF version)

© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2014

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

## Table of Contents

|                                                                                         |    |
|-----------------------------------------------------------------------------------------|----|
| Overview.....                                                                           | 1  |
| Registration Decision for Fluopyram .....                                               | 1  |
| What Does Health Canada Consider When Making a Registration Decision? .....             | 1  |
| What Is Fluopyram? .....                                                                | 2  |
| Health Considerations.....                                                              | 2  |
| Risks in Residential and Other Non-Occupational Environments .....                      | 4  |
| Environmental Considerations .....                                                      | 4  |
| Value Considerations.....                                                               | 5  |
| Measures to Minimize Risk.....                                                          | 5  |
| What Additional Scientific Information Is Being Requested? .....                        | 6  |
| Other Information .....                                                                 | 7  |
| Science Evaluation.....                                                                 | 9  |
| 1.0 The Active Ingredient, Its Properties and Uses .....                                | 9  |
| 1.1 Identity of the Active Ingredient .....                                             | 9  |
| 1.2 Physical and Chemical Properties of the Active Ingredients and End-use Product..... | 9  |
| 1.3 Directions for Use .....                                                            | 11 |
| 1.4 Mode of Action .....                                                                | 12 |
| 2.0 Methods of Analysis .....                                                           | 12 |
| 2.1 Methods for Analysis of the Active Ingredient.....                                  | 12 |
| 2.2 Method for Formulation Analysis.....                                                | 12 |
| 2.3 Methods for Residue Analysis .....                                                  | 12 |
| 3.0 Impact on Human and Animal Health .....                                             | 13 |
| 3.1 Toxicology Summary.....                                                             | 13 |
| 3.1.1 <i>Pest Control Products Act</i> Hazard Characterization .....                    | 17 |
| 3.2 Acute Reference Dose (ARfD) .....                                                   | 18 |
| 3.3 Acceptable Daily Intake (ADI) .....                                                 | 18 |
| 3.4 Occupational and Residential Risk Assessment.....                                   | 19 |
| 3.4.1 Toxicological Endpoints .....                                                     | 19 |
| 3.4.2 Occupational Exposure and Risk.....                                               | 21 |
| 3.4.3 Residential Exposure and Risk Assessment .....                                    | 24 |
| 3.5 Food Residues Exposure Assessment .....                                             | 24 |
| 3.5.1 Residues in Plant and Animal Foodstuffs.....                                      | 24 |
| 3.5.2 Exposure from Drinking Water .....                                                | 25 |
| 3.5.3 Dietary Risk Assessment .....                                                     | 26 |
| 3.5.4 Aggregate Exposure and Risk.....                                                  | 27 |
| 3.5.5 Maximum Residue Limits.....                                                       | 28 |
| 4.0 Impact on the Environment.....                                                      | 29 |
| 4.1 Fate and Behaviour in the Environment.....                                          | 29 |
| 4.2 Environmental Risk Characterization .....                                           | 29 |
| 4.2.1 Risks to Terrestrial Organisms.....                                               | 30 |
| 4.2.2 Risks to Aquatic Organisms.....                                                   | 33 |

|            |                                                                                                                                                     |    |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|----|
| 5.0        | Value.....                                                                                                                                          | 36 |
| 5.1        | Effectiveness Against Pests.....                                                                                                                    | 36 |
| 5.1.1      | Acceptable Efficacy Claims.....                                                                                                                     | 36 |
| 5.2        | Phytotoxicity .....                                                                                                                                 | 40 |
| 5.3        | Economics .....                                                                                                                                     | 40 |
| 5.4        | Sustainability.....                                                                                                                                 | 40 |
| 5.4.1      | Survey of Alternatives .....                                                                                                                        | 40 |
| 5.4.2      | Compatibility with Current Management Practices Including Integrated Pest Management.....                                                           | 41 |
| 5.4.3      | Information on the Occurrence or Possible Occurrence of the Development of Resistance .....                                                         | 41 |
| 5.4.4      | Contribution to Risk Reduction and Sustainability .....                                                                                             | 41 |
| 6.0        | Pest Control Product Policy Considerations.....                                                                                                     | 42 |
| 6.1        | Toxic Substances Management Policy Considerations.....                                                                                              | 42 |
| 6.2        | Formulants and Contaminants of Health or Environmental Concern .....                                                                                | 43 |
| 7.0        | Summary.....                                                                                                                                        | 43 |
| 7.1        | Human Health and Safety .....                                                                                                                       | 43 |
| 7.2        | Environmental Risk.....                                                                                                                             | 44 |
| 7.3        | Value .....                                                                                                                                         | 44 |
| 8.0        | Regulatory Decision.....                                                                                                                            | 45 |
|            | List of Abbreviations .....                                                                                                                         | 47 |
| Appendix I | Tables and Figures .....                                                                                                                            | 51 |
| Table 1    | Residue Analysis.....                                                                                                                               | 51 |
| Table 2    | Toxicity Profile of Luna Privilege .....                                                                                                            | 52 |
| Table 3    | Toxicity Profile of Luna Tranquility Fungicide.....                                                                                                 | 52 |
| Table 4    | Toxicity Profile of Propulse Fungicide.....                                                                                                         | 52 |
| Table 5    | Toxicity Profile of Technical Fluopyram Fungicide .....                                                                                             | 53 |
| Table 6    | Toxicology Endpoints for Use in Health Risk Assessment for Fluopyram.....                                                                           | 60 |
| Table 7    | Exposure Estimates for Mixers/Loaders/Applicators .....                                                                                             | 60 |
| Table 8    | Non-Cancer Exposure and Risk Estimates for Mixer/Loader/Applicators Handling Fluopyram.....                                                         | 61 |
| Table 9    | Cancer Exposure and Risk Estimates for Mixer/Loader/Applicators Handling Fluopyram.....                                                             | 61 |
| Table 10   | Non-Cancer Postapplication Exposure and Risk Estimates for Fluopyram .....                                                                          | 62 |
| Table 11   | Cancer Postapplication Exposure and Risk Estimates for Fluopyram.....                                                                               | 62 |
| Table 12   | Major Groundwater and Surface Water Model Inputs for Level 1, Level 2 and Level 2 Restricted Application Assessments.....                           | 63 |
| Table 13   | Level 1 and Level 2 Estimated Environmental Concentrations of Fluopyram in Potential Drinking Water Sources .....                                   | 63 |
| Table 14   | Level 2 Additional Modelling - Restricted Application Estimated Environmental Concentrations of Fluopyram in Potential Drinking Water Sources ..... | 64 |
| Table 15   | Groundwater EECs ( $\mu\text{g/L}$ ) Averaged over Five Time Periods*.....                                                                          | 64 |
| Table 16   | Number of Days When EECs Exceed $2 \mu\text{g/L}$ for All 11 Groundwater Scenarios, Assuming Applications over One, Two or Three Years.....         | 65 |
| Table 17   | Groundwater EECs ( $\mu\text{g/L}$ )* Averaged over Seventy Years.....                                                                              | 65 |

|           |                                                                                                                                             |     |
|-----------|---------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Table 18a | Nature of the Residues in Plant Matrices .....                                                                                              | 65  |
| Table 18b | Nature of the Residues in Plant Matrices: Confined Accumulation in Rotational Crops .....                                                   | 75  |
| Table 18c | Nature of the Residues in Livestock .....                                                                                                   | 81  |
| Table 18d | Freezer Storage Stability .....                                                                                                             | 87  |
| Table 18e | Crop Field Trials and Residue Decline .....                                                                                                 | 87  |
| Table 18f | Residue Data in Rotational Crops .....                                                                                                      | 91  |
| Table 18g | Residues in Processed Food and Feed.....                                                                                                    | 94  |
| Table 18h | Livestock Feeding .....                                                                                                                     | 97  |
| Table 19  | Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment                                                                   | 99  |
| Table 20  | Summary of Physico-Chemical Properties of Fluopyram Relevant to the Environment.....                                                        | 100 |
| Table 21  | Fate and Behaviour in the Terrestrial Environment.....                                                                                      | 101 |
| Table 22  | Fate and Behaviour in the Aquatic Environment.....                                                                                          | 102 |
| Table 23  | Maximum Concentrations of Transformation Products in Soil and Water .....                                                                   | 103 |
| Table 24  | Structure and Properties of Parent Compound and Transformation Products .....                                                               | 103 |
| Table 25  | Screening Level EECs* (Luna Privilege).....                                                                                                 | 104 |
| Table 26  | Level 1 Aquatic Eco-Scenario Modelling EECs for Fluopyram in a Water Body of 0.15 m Deep Excluding Spray Drift .....                        | 104 |
| Table 27  | EECs in Vegetation and Insects after a Direct Over-Spray <sup>1</sup> (Luna Privilege) .....                                                | 104 |
| Table 28  | Effects on Terrestrial Organisms .....                                                                                                      | 105 |
| Table 29  | Screening Level Risk Assessment to Terrestrial Organisms (Luna Privilege).....                                                              | 106 |
| Table 30  | Screening Level Risk Assessment to Wild Birds .....                                                                                         | 106 |
| Table 31  | Expanded Screening Level Reproductive Risk Assessment to Wild Birds for On-Field and Off-Field Scenarios (Luna Privilege).....              | 107 |
| Table 32  | Refined Assessment of Reproductive Risk to Wild Birds for On-Field and Off-Field Scenarios (Luna Privilege) .....                           | 107 |
| Table 33  | Screening Level Risk Assessment to Mammals (Luna Privilege).....                                                                            | 108 |
| Table 34  | Expanded Screening Level Assessment of Reproductive Risk to Mammals with Same Endpoints (Luna Privilege).....                               | 108 |
| Table 35  | Refined Assessment of Reproductive Risk to Mammals (Luna Privilege) .....                                                                   | 109 |
| Table 36  | Screening Level Risk Assessment to Terrestrial Plants (Luna Privilege) .....                                                                | 110 |
| Table 37  | Refined Risk Assessment to Terrestrial Plants (Luna Privilege).....                                                                         | 110 |
| Table 38  | Screening Level EEC* for Fluopyram (Luna Tranquility Fungicide).....                                                                        | 110 |
| Table 39  | Maximum EECs Fluopyram in Vegetation and Insects after a Direct Over-Spray (Luna Tranquility Fungicide).....                                | 111 |
| Table 40  | Screening Level Risk Assessment to Wild Birds (Luna Tranquility Fungicide)..                                                                | 111 |
| Table 41  | Expanded Screening Level Reproductive Risk Assessment for Wild Birds for On-Field and Off-Field Scenarios (Luna Tranquility Fungicide)..... | 111 |
| Table 42  | Refined Assessment of Reproductive Risk for Wild Birds (Luna Tranquility Fungicide) .....                                                   | 112 |
| Table 43  | Screening Level Risk Assessment to Mammals (Luna Tranquility Fungicide) ...                                                                 | 113 |
| Table 44  | Expanded Screening Level Reproductive Risk Assessment for Mammals (Luna Tranquility Fungicide) .....                                        | 113 |
| Table 45  | Refined Assessment of Reproductive Risk for Mammals (Luna Tranquility Fungicide) .....                                                      | 113 |

|             |                                                                                                                                                                          |     |
|-------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|
| Table 46    | Screening Level Risk Assessment to Terrestrial Plants (Luna Tranquility Fungicide) .....                                                                                 | 114 |
| Table 47    | Screening Level Risk Assessment to Wild Birds (Propulse Fungicide).....                                                                                                  | 114 |
| Table 48    | Expanded Screening Level Reproductive Risk Assessment for Wild Birds (Propulse Fungicide).....                                                                           | 114 |
| Table 49    | Refined Reproductive Risk Assessment for Wild Birds (Propulse Fungicide) ....                                                                                            | 115 |
| Table 50    | Screening Level Risk Assessment to Terrestrial Plants (Propulse Fungicide).....                                                                                          | 115 |
| Table 51    | Effects on Aquatic Organisms .....                                                                                                                                       | 116 |
| Table 52    | Screening Level Risk Assessment to Aquatic Organisms (Luna Privilege).....                                                                                               | 118 |
| Table 53    | Refined Risk Assessment to Amphibians: Run off (Luna Privilege) .....                                                                                                    | 118 |
| Table 54    | Refined Risk Assessment to Amphibians: Spray Drift (Luna Privilege) .....                                                                                                | 119 |
| Table 55    | Screening Level and Refined Risk Assessment to Amphibians: Spray Drift from Aerial Application (Potato).....                                                             | 119 |
| Table 56    | Screening Level Risk Assessment to Amphibians (Propulse Fungicide).....                                                                                                  | 119 |
| Table 57    | Refined Risk Assessment to Amphibians: Run Off (Propulse Fungicide).....                                                                                                 | 119 |
| Table 58    | Refined Risk Assessment to Amphibians: Spray Drift (Propulse Fungicide) .....                                                                                            | 119 |
| Table 59    | Luna Privilege Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported.....                                                                       | 120 |
| Table 60    | Luna Tranquility Fungicide Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported.....                                                           | 121 |
| Table 61    | Propulse Fungicide Use (Label) Claims Proposed by Applicant and Whether Acceptable or Unsupported.....                                                                   | 121 |
| Table 62    | Active Ingredients Currently Registered for Management of Crop Diseases on the Luna Privilege Fungicide, Luna Tranquility Fungicide, and Propulse Fungicide Labels ..... | 121 |
| Table 63    | TSMP considerations-comparison to TSMP Track 1 criteria.....                                                                                                             | 124 |
| Appendix II | Supplemental Maximum Residue Limit Information—International Situation and Trade Implications .....                                                                      | 127 |
| Table 1     | Differences Between MRLs in Canada and in Other Jurisdictions .....                                                                                                      | 127 |
| References  | .....                                                                                                                                                                    | 129 |

# 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<sup>1</sup> 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<sup>2</sup> when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

---

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

<sup>2</sup> "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](http://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,<sup>3</sup> 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](mailto:pmra.infoserv@hc-sc.gc.ca)).

---

<sup>3</sup> As per subsection 28(1) of the *Pest Control Products Act*.

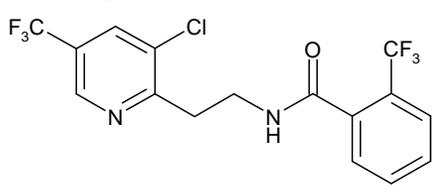


# Science Evaluation

## Fluopyram

### 1.0 The Active Ingredient, Its Properties and Uses

#### 1.1 Identity of the Active Ingredient

|                                                                     |                                                                                                                     |
|---------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| <b>Active substance</b>                                             | Fluopyram                                                                                                           |
| <b>Function</b>                                                     | Fungicide                                                                                                           |
| <b>Chemical name</b>                                                |                                                                                                                     |
| <b>1. International Union of Pure and Applied Chemistry (IUPAC)</b> | <i>N</i> -{2-[3-chloro-5-(trifluoromethyl)-2-pyridyl]ethyl}- $\alpha,\alpha,\alpha$ -trifluoro- <i>o</i> -toluamide |
| <b>2. Chemical Abstracts Service (CAS)</b>                          | Benzamide, <i>N</i> -[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)-                       |
| <b>CAS number</b>                                                   | 658066-35-4                                                                                                         |
| <b>Molecular formula</b>                                            | C <sub>16</sub> H <sub>11</sub> ClF <sub>6</sub> N <sub>2</sub> O                                                   |
| <b>Molecular weight</b>                                             | 396.72 g/mol                                                                                                        |
| <b>Structural formula</b>                                           |                                 |
| <b>Purity of the active ingredient</b>                              | 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      | $1.2 \times 10^{-6}$ Pa (20°C)                             |
| Henry's law constant at 20°C | $2.98 \times 10^{-5}$ Pa×m <sup>3</sup> ×mol <sup>-1</sup> |

| Property                                                                 | Result                                                                                                                       |
|--------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------|
| Ultraviolet (UV)-visible spectrum                                        | Acetonitrile:                                                                                                                |
|                                                                          | $\lambda_{\max}$ [nm] $\epsilon$ [L mol <sup>-1</sup> cm <sup>-1</sup> ]                                                     |
|                                                                          | 216                                              14877                                                                       |
|                                                                          | 270                                              4332.18                                                                     |
|                                                                          | Acetonitrile pH = 2:                                                                                                         |
|                                                                          | $\lambda_{\max}$ [nm] $\epsilon$ [L mol <sup>-1</sup> cm <sup>-1</sup> ]                                                     |
|                                                                          | 208                                              16570.99                                                                    |
|                                                                          | 270                                              4399.62                                                                     |
|                                                                          | Acetonitrile pH = 10:                                                                                                        |
|                                                                          | $\lambda_{\max}$ [nm] $\epsilon$ [L mol <sup>-1</sup> cm <sup>-1</sup> ]                                                     |
|                                                                          | 208                                              16892.34                                                                    |
|                                                                          | 270                                              4383.76                                                                     |
|                                                                          | Water                                                                                                                        |
| $\lambda_{\max}$ [nm] $\epsilon$ [L mol <sup>-1</sup> cm <sup>-1</sup> ] |                                                                                                                              |
| 270                                              4577.053                |                                                                                                                              |
| Solubility in water at 20°C                                              | 16 mg/L (distilled water)<br>15 mg/L (pH 4)<br>16 mg/L (pH 7)<br>15 mg/L (pH 9)                                              |
| Solubility in organic solvents at 20°C                                   | <u>Solvent</u> <u>Solubility (g/L)</u>                                                                                       |
|                                                                          | acetone                                              >250                                                                    |
|                                                                          | dichlorethane                                              >250                                                              |
|                                                                          | dimethyl sulfoxide                                              >250                                                         |
|                                                                          | ethyl acetate                                              >250                                                              |
|                                                                          | n-heptane                                              0.66                                                                  |
|                                                                          | methanol                                              >250                                                                   |
|                                                                          | toluene                                              62.2                                                                    |
| <i>n</i> -Octanol-water partition coefficient ( $K_{ow}$ )               | log $K_{ow}$ = 3.3 at 20°C                                                                                                   |
| Dissociation constant (p <i>K</i> <sub>a</sub> )                         | No dissociation observed between pH 2 and 12                                                                                 |
| Stability<br>(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<br>Pyrimethanil 375 g/L                                       | Fluopyram 200 g/L<br>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                                                                   |
| Explosibility                      | 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<sub>2</sub> 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<sub>50</sub> 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](http://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  $1.72 \times 10^{-2} \text{ (mg/kg bw/day)}^{-1}$ .

### **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<sup>2</sup> 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:

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

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 [ $Q_1^* = 1.72 \times 10^{-2} (\text{mg/kg bw/day})^{-1}$ ].

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

Cancer risks for farmers and custom applicators mixing/loading and applying products containing fluopyram to all approved crops are below  $1 \times 10^{-5}$  (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:

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

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.

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

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 [ $Q_1^* = 1.72 \times 10^{-2} \text{ (mg/kg bw/day)}^{-1}$ ].

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

Cancer risks for worker entering fields treated with fluopyram are below  $1 \times 10^{-5}$  (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  $1.6 \times 10^{-5}$  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 ( $2 \times 250$  g a.i./ha at a 14-day interval). For reservoir modelling, PEI-potato was run with the use pattern modeled at Level 1 ( $2 \times 250$  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 ( $2 \times 250$  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<sup>th</sup> 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  $1 \times 10^{-6}$  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<sup>th</sup> 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**

| <b>Commodity</b>                                                                                                                                                                                                                                                                                                                         | <b>Recommended MRL (ppm)</b> |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| 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 – Tuberos 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 ( $RQ = \text{exposure}/\text{toxicity}$ ), 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:  $EDE = (FIR/bw) \times EEC$ , 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<sub>25</sub> 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)<sub>50</sub> 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<sub>50</sub> 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 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<sup>4</sup> 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.<sup>5</sup>

---

<sup>4</sup> DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

<sup>5</sup> 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*.<sup>6</sup> The list is used as described in the PMRA Notice of Intent NOI2005-01<sup>7</sup> 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.

---

<sup>6</sup> *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.*

<sup>7</sup> 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 <i>O</i> -deethylation                                          |
| BW/bw            | body weight                                                                        |
| bwg              | body weight gain                                                                   |
| CAF              | composite assessment factor                                                        |
| CAS              | Chemical Abstracts Service                                                         |
| cm               | centimetres                                                                        |
| cm <sup>2</sup>  | centimetres square                                                                 |
| cm <sup>3</sup>  | cubic centimetres                                                                  |
| CO <sub>2</sub>  | carbon dioxide                                                                     |
| d                | day(s)                                                                             |
| DFOP             | Double-First-Order in Parallel                                                     |
| DFR              | dislodgeable foliar residue                                                        |
| DT <sub>50</sub> | dissipation time 50% (the time required to observe a 50% decline in concentration) |
| DT <sub>75</sub> | dissipation time 75% (the time required to observe a 75% decline in concentration) |
| DT <sub>90</sub> | dissipation time 90% (the time required to observe a 90% decline in concentration) |
| dw               | dry weight                                                                         |
| EC <sub>05</sub> | effective concentration on 5% of the population                                    |
| EC <sub>25</sub> | effective concentration on 25% of the population                                   |
| EC <sub>50</sub> | effective concentration on 50% of the population                                   |
| EDE              | estimated daily exposure                                                           |
| EEC              | estimated environmental exposure concentration                                     |
| ER <sub>50</sub> | effective rate on 50% of the population                                            |
| EROD             | 7-ethoxyresorufin <i>O</i> -deethylation                                           |
| F <sub>1</sub>   | first generation                                                                   |
| F <sub>2</sub>   | 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 <sub>d</sub>   | soil-water partition coefficient                                     |
| kg               | kilogram                                                             |
| K <sub>oc</sub>  | organic-carbon partition coefficient                                 |
| K <sub>ow</sub>  | octanol-water partition coefficient                                  |
| L                | litre                                                                |
| LADD             | lifetime average daily dose                                          |
| LC <sub>50</sub> | lethal concentration 50%                                             |
| LD               | low dose                                                             |
| LD <sub>50</sub> | 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 <sub>50</sub> | lethal rate 50%                                                      |
| m                | metre(s)                                                             |
| m <sup>3</sup>   | 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                     |
| $pK_a$ | dissociation constant                   |
| PMRA   | Pest Management Regulatory Agency       |
| ppm    | parts per million                       |
| PROD   | pentoxyresorufin <i>O</i> -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<br>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/<br>Sediment | GM-002-S07-01<br>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 | HPLC-MS/MS  | 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;<br>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<br>Wistar rats                   | Female LD <sub>50</sub> > 2000 mg/kg bw<br>Low toxicity | 1599335 |
| Acute dermal toxicity<br>Wistar rats                 | LD <sub>50</sub> > 2000 mg/kg bw<br>Low toxicity        | 1599336 |
| Acute inhalation toxicity (nose-only)<br>Wistar rats | LC <sub>50</sub> > 2.09 mg/L<br>Low toxicity            | 1599337 |
| Dermal irritation<br>NZW rabbits                     | MAS = 0, MIS = 0<br>Non-irritating                      | 1599338 |
| Eye irritation<br>NZW rabbits                        | MAS = 0, MIS = 5.3<br>Minimally irritating              | 1520933 |
| Dermal sensitization (LLNA)<br>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<br>Sprague Dawley rats           | Female LD <sub>50</sub> > 5000 mg/kg bw<br>Low toxicity | 1670082 |
| Acute dermal toxicity<br>Wistar rats                 | LD <sub>50</sub> > 2000 mg/kg bw<br>Low toxicity        | 1670083 |
| Acute inhalation toxicity (nose-only)<br>Wistar rats | LC <sub>50</sub> ≥ 2.0 mg/L<br>Low toxicity             | 1670084 |
| Dermal irritation<br>NZW rabbits                     | MAS = 0, MIS = 0<br>Non-irritating                      | 1670085 |
| Eye irritation<br>NZW rabbits                        | MAS = 0, MIS = 2<br>Non-irritating                      | 1670086 |
| Dermal sensitization (LLNA)<br>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<br>Sprague Dawley rats           | Female LD <sub>50</sub> : >5000 mg/kg bw<br>Low toxicity | 1670748 |
| Acute dermal toxicity<br>Sprague Dawley rats         | LD <sub>50</sub> : >5050 mg/kg bw<br>Low toxicity        | 1670747 |
| Acute inhalation toxicity (nose-only)<br>Wistar rats | LC <sub>50</sub> : ≥2.2 mg/L<br>Low toxicity             | 1670744 |

| Study Type/Animal                             | Study Results                      | PMRA #  |
|-----------------------------------------------|------------------------------------|---------|
| Dermal irritation<br>NZW rabbits              | MAS = 0, MIS = 0<br>Non-irritating | 1670745 |
| Eye irritation<br>NZW rabbits                 | MAS = 0, MIS = 0<br>Non-irritating | 1670746 |
| Dermal sensitization (Buehler)<br>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/<br>toxicokinetics (single and<br>repeat dose, oral, gavage)<br>Wistar rat | <p><b>Rate and extent of absorption and excretion:</b> 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 (<math>t_{max}</math>) 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 <math>t_{max}</math> values of 0.7 h and 3.3 h for SOLD males and females, respectively. The <math>C_{max}</math> 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.</p> <p>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.</p> <p><b>Distribution / target organ(s):</b> 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.</p> <p><b>Toxicologically significant compound(s):</b> Fluopyram was extensively</p> | 1599513,<br>1599517,<br>1599524,<br>1599526,<br>1599529 |

| Study Type/Animal                                       | Study Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | PMRA #  |
|---------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
|                                                         | <p>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).</p> <p>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.</p> |         |
| Acute oral toxicity<br>Wistar rats                      | Female LD <sub>50</sub> : >2000 mg/kg bw<br>Low Toxicity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 1599564 |
| Acute dermal toxicity<br>Wistar rats                    | LD <sub>50</sub> : >2000 mg/kg bw<br>Low Toxicity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 1599563 |
| Acute inhalation toxicity<br>(nose-only)<br>Wistar rats | LC <sub>50</sub> : >5.1 mg/L air<br>Low Toxicity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 1599559 |
| Skin irritation<br>NZW rabbits                          | MAS = 0, MIS = 0<br>Non-irritating                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1599561 |
| Eye Irritation<br>NZW rabbits                           | MAS = 1.8, MIS = 8.7<br>Minimally irritating                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1599558 |
| Skin Sensitization<br>(LLNA)<br>CBA/J mice              | Non-sensitizer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1599573 |
| 4-week dermal toxicity<br>Wistar rat                    | <p>Systemic NOAEL = 300 mg/kg bw/day<br/>Dermal NOAEL = 1000 mg/kg bw/day</p> <p>1000 mg/kg bw/day:<br/>↑ prothrombin time, ↑ cholesterol, ↑ liver weights, ↑ minimal centrilobular and mid-zonal hepatocellular hypertrophy<br/>No treatment-related dermal effects.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1599533 |
| 28-day dietary<br>C57BL/6J mouse                        | <p>Range-finding</p> <p>24.7/31.1 mg/kg bw/day ♂/♀:<br/>↑ liver weights, ↑ centrilobular hepatocellular hypertrophy</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 1599579 |

| Study Type/Animal                | Study Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | PMRA #  |
|----------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
|                                  | <p>162/197 mg/kg bw/day ♂/♀:<br/>           ↑ liver weights, ↑ enlarged &amp; dark livers, ↑ centrilobular hypertrophy, ↑ focal necrosis in liver; ↑ single cell hepatocellular necrosis ♂; ↑ hypertrophy of zona fasciculata in adrenals ♀</p> <p>747/954 mg/kg bw/day ♂/♀ (exceeded MTD):<br/>           ↑ 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 &amp; enlarged livers, reduced thymic size, distended abdomen, adrenal hypertrophy, vacuolation, degeneration/necrosis of zona fasciculata, perivascular &amp; intra-alveolar hemorrhage of lungs, degeneration of pulmonary veins, erythroid extramedullary hematopoiesis in spleen, ↓ cellularity &amp; 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 ♂</p> <p>Surviving females:<br/>           Distended abdomen, ↑ total cholesterol, total protein, ↑ ALAT, ↑ enlarged &amp; 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</p> |         |
| 28-day dietary<br>Wistar rat     | <p>Range-finding</p> <p>≥31.0/36.1 mg/kg bw/day ♂/♀:<br/>           ↑ 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 ♂</p> <p>254/263 mg/kg bw/day ♂/♀:<br/>           ↓ 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 ♀</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1599574 |
| 28-day gavage<br>Beagle dog      | <p>Supplemental</p> <p>750 mg/kg bw/day:<br/>           ↑ 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 ♂</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1599578 |
| 90-day dietary<br>C57BL/6J mouse | <p>NOAEL = 26.6/32.0 mg/kg bw/day ♂/♀</p> <p>188/216 mg/kg bw/day ♂/♀:<br/>           ↑ ALAT, ↑ ALK, ↑ ASAT, ↓ albumin, ↑ adrenal weight, ↑ dark livers, ↑ focal necrosis in liver, ↑ cortical vacuolation in adrenals, ↓ cortical ceroid pigment in adrenals</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 1599556 |
| 90-day dietary<br>Wistar rat     | <p>NOAEL = 12.5/14.6 mg/kg bw/day ♂/♀</p> <p>≥60.5/70.1 mg/kg bw/day ♂/♀:<br/>           ↓ bilirubin, ↑ TSH, ↑ T3, ↑ T4, pale kidneys, dark livers, ↑ prominent lobulation in liver, positive cysts cortico-medullary junction, ↑ positive</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 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<br>Dog                                                                | NOAEL = 28.5/32.9 mg/kg bw/day ♂/♀<br><br>≥171/184 mg/kg bw/day ♂/♀:<br>↓ 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<br>Beagle dog                                                       | NOAEL = 13.2/14.4 mg/kg bw/day ♂/♀<br><br>67.6/66.1 mg/kg bw/day ♂/♀:<br>↓ bwg wk 1, ↓ FC, ↑ ALK, ↑ GGT; ↑ diffuse hypertrophy of follicular epithelium of thyroid, ↑ diffuse centrilobular hepatocellular hypertrophy ♂; ↑ thyroid weights ♀                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1599548 |
| 2-year dietary, chronic<br>toxicity / oncogenicity<br>(combined)<br>Wistar rat       | Chronic toxicity:<br>NOAEL = 1.2/1.7 mg/kg bw/day ♂/♀<br><br>Liver carcinoma and adenoma ♀<br><br>52-week sacrifice:<br>6.0/8.6 mg/kg bw/day ♂/♀:<br>↑ 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 ♂<br><br>Main group:<br>6.0/8.6 mg/kg bw/day ♂/♀:<br>↑ 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<br>toxicity / oncogenicity<br>(combined)<br>C57BL/6J mouse | Chronic toxicity:<br>NOAEL = 4.2/5.3 mg/kg bw/day ♂/♀<br><br>Thyroid follicular cell adenoma ♂<br><br>52-week sacrifice:<br>20.9/26.8 mg/kg bw/day (♂/♀):<br>↑ liver weight; ↑ enlarged liver, ↑ focal/multifocal thyroid follicular cell hyperplasia ♂<br><br>Main group:<br>20.9/26.8 mg/kg bw/day (♂/♀):<br>↑ 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)<br>Wistar rat Supplemental | Supplemental<br><br>Parental effects<br>≥49.6/57.7 mg/kg bw/day ♂/♀:<br>↑ liver weights; ↑ kidney weight ♂<br><br>102.1/118.2 mg/kg bw/day ♂/♀:<br>↓ thymus weight; ↓ prematuring bwg ♀                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1599823 |
| Multi-generation dietary<br>Wistar rat                            | Parental<br>NOAEL = 13.9/16.8 mg/kg bw/day ♂/♀<br>Reproductive<br>NOAEL = 82.4/95.6 mg/kg bw/day ♂/♀<br>Offspring<br>NOAEL = 13.9/16.8 mg/kg bw/day ♂/♀<br><br>Parental effects<br>82.4/95.6 mg/kg bw/day ♂/♀:<br>↑ centrilobular hepatocellular hypertrophy; ↑ protein droplet nephropathy and lymphocytic infiltration, ↑ cytoplasmic vacuolization in adrenals F <sub>1</sub> , ↑ kidney weights F <sub>0</sub> & F <sub>1</sub> ♂; ↓ bw prematuring & gestation F <sub>0</sub> , ↓ bwg prematuring F <sub>0</sub> & F <sub>1</sub> , ↑ cholesterol F <sub>1</sub> , ↑ WBC F <sub>1</sub> , ↑ monocyte absolute cell counts F <sub>1</sub> , ↑ liver weights F <sub>0</sub> & F <sub>1</sub> , ↓ spleen weights F <sub>0</sub> & F <sub>1</sub> , ↑ alveolar macrophages in lungs F <sub>1</sub> ♀<br><br>Offspring effects<br>82.4/95.6 mg/kg bw/day ♂/♀:<br>↓ bw F <sub>1</sub> & F <sub>2</sub> , ↓ bwg F <sub>1</sub> & F <sub>2</sub> , ↓ spleen and thymus weights F <sub>2</sub> | 1599824 |
| Developmental toxicity<br>Sprague Dawley rat                      | Maternal<br>NOAEL = 30 mg/kg bw/day<br><br>Developmental<br>NOAEL = 150 mg/kg bw/day<br><br>Maternal effects:<br>≥150 mg/kg bw/day:<br>↓ bwg, ↓ corrected bwg to gravid uterine weight, ↓ FC, ↑ abs. liver weight, ↑ centrilobular hepatocellular hypertrophy<br><br>Developmental effects:<br>450 mg/kg bw/day:<br>↓ fetal weights, ↑ thymic remnant present, ↑ skeletal variations<br>No evidence of teratogenicity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1599610 |
| Developmental toxicity<br>NZW rabbit                              | Maternal<br>NOAEL = 25 mg/kg bw/day<br><br>Developmental effects<br>NOAEL = 25 mg/kg bw/day<br><br>Maternal effects:<br>75 mg/kg bw/day:<br>↓ bw, ↓ bwg, ↓ corrected bwg to gravid uterine weight, ↓ FC<br><br>Developmental effects:<br>75 mg/kg bw/day:<br>↓ fetal weights, ↑ runts (bw < 28.0 g)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1599571 |

| Study Type/Animal                                                                                                                                                            | Study Results                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | PMRA #  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Acute Neurotoxicity<br>Wistar rat                                                                                                                                            | <p>Main study:<br/>NOAEL = 125 mg/kg bw/not established ♂/♀</p> <p>Supplemental study (female only):<br/>Female NOAEL = 50 mg/kg bw</p> <p>Main study:<br/>≥125 mg/kg bw:<br/>↓ session motor activity, ↓ session locomotor activity ♀</p> <p>≥ 500 mg/kg bw:<br/>↓ session motor activity, ↓ session locomotor activity ♂; ↓ body temperature,<br/>↓ vocalization during removal ♀</p> <p>Supplemental:<br/>100 mg/kg bw:<br/>↓ session motor activity, ↓ session locomotor activity ♀</p> | 1599618 |
| Subchronic Neurotoxicity<br>Wistar rat                                                                                                                                       | <p>Systemic toxicity:<br/>NOAEL = 33.2/41.2 mg/kg bw/day ♂/♀</p> <p>164.2/197.1 mg/kg bw/day ♂/♀:<br/>↓ bw, ↓ bwg, ↑ cholesterol, ↑ bilateral retinal degeneration; ↓ FC ♂; ↑ TG, ↑ thyroid weights ♀</p>                                                                                                                                                                                                                                                                                   | 1599534 |
| Gene mutations in<br>bacteria in vitro                                                                                                                                       | Negative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1599580 |
| Gene mutations in<br>bacteria in vitro                                                                                                                                       | Negative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1599553 |
| In vitro mammalian<br>clastogenicity<br>Chromosome aberrations                                                                                                               | Negative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1599552 |
| In vitro mammalian cell<br>assay<br>V79/HPRT forward<br>mutation                                                                                                             | Negative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1229493 |
| In vivo cytogenetics<br>Micronucleus assay                                                                                                                                   | Negative                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1229494 |
| 3-day toxicity study in<br>male C57BL/6J mouse –<br>pharmacokinetic<br>investigations of the<br>clearance of intravenous<br>(iv)-administered <sup>125</sup> I-<br>thyroxine | <p>Non-guideline</p> <p>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.</p>                                                                                                                                                                                       | 1654272 |
| 3-day toxicity study in<br>male C57BL/6J mice -<br>QPCR investigations of<br>gene transcripts in the<br>liver                                                                | <p>Non-guideline</p> <p>Fluopyram (300 mg/kg bw/day):<br/>↑ liver weight, ↑ expression of the following genes:<br/>Cyp1a, Cyp2b, Cyp 3a, Sult1a1, Sult 2a2, Suln, Ugt1a1, Ugt2b1, Ugt2b5</p> <p>PB (80 mg/kg bw):<br/>Reduced motor activity<br/>↑ liver weight, ↑ expression of the following genes:<br/>Cyp2b, Cyp 3a, Sult1a1, Sult 2a2, Suln, Ugt1a1, Ugt2b1, Ugt2b5</p>                                                                                                                | 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 | <p>Non-guideline</p> <p>3 day exposure<br/>308 mg/kg bw/day:<br/>↓ 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</p> <p>Phenobarbital at 80 mg/kg bw/day:<br/>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</p> <p>14 day exposure<br/>314 mg/kg bw/day:<br/>↓ 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</p> <p>Phenobarbital at 80 mg/kg bw/day:<br/>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</p> | 1599576,<br>1599803 |
| 7-day toxicity in female Wistar rats (dietary) fluopyram vs. phenobarbital                                               | <p>Non-guideline</p> <p>193 mg/kg bw/day:<br/>↓ 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</p> <p>Phenobarbital at 80 mg/kg bw/day:<br/>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</p>                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1599741,<br>1599802 |
| In vitro studies with hog thyroid microsomes on the potential interactions with thyroid peroxidase-catalyzed reactions   | <p>Non-guideline</p> <p>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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 1599551             |
| <b>METABOLITE – AE C656948-pyridyl-carboxylic acid (AE 657188)</b>                                                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                     |
| Acute oral toxicity Wistar rats                                                                                          | Female LD <sub>50</sub> : >2000 mg/kg bw<br>Low Toxicity                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 1599809             |
| 28-day dietary Sprague Dawley rat                                                                                        | NOAEL = 1574/162 mg/kg bw/day ♂/♀<br><br>1581 mg/kg bw/day ♀:<br>↓ bwg, FC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 1599612             |

| Study Type/Animal                              | Study Results                                                                                                                                                                   | PMRA #  |
|------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| Bacterial mutation assay                       | Negative                                                                                                                                                                        | 1599630 |
| In vitro mammalian cell forward mutation assay | Precipitation observed at $\geq 4000 \mu\text{g/mL}$ in the absence of S9 mix and at $5000 \mu\text{g/mL}$ in the presence of S9 mix (data were not interpretable).<br>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 <sup>1</sup> or Target MOE |
|------------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|--------------------------------|
| Acute dietary general population                     | Rat acute neurotoxicity study                                                   | NOAEL = 50 mg/kg bw<br>Reduced motor and locomotor activity                               | 100                            |
|                                                      | <b>Acute reference dose</b> = 0.5 mg/kg bw                                      |                                                                                           |                                |
| Repeated dietary                                     | Rat chronic toxicity/carcinogenicity study                                      | NOAEL = 1.2 mg/kg bw/day<br>Numerous effects, primarily in liver, kidney, thyroid and eye | 100                            |
|                                                      | <b>Acceptable daily intake</b> = 0.012 mg/kg bw/day                             |                                                                                           |                                |
| Short- and intermediate term dermal <sup>2</sup>     | Rat 28 day dermal toxicity study                                                | NOAEL = 300 mg/kg bw/day<br>Clinical chemistry and liver effects                          | 100                            |
| Long-term dermal <sup>2</sup>                        | Rat chronic toxicity/carcinogenicity study                                      | NOAEL = 1.2 mg/kg bw/day<br>Numerous effects, primarily in liver, kidney, thyroid and eye | 100                            |
| Short- and intermediate-term inhalation <sup>3</sup> | Rat 90 day oral toxicity study                                                  | NOAEL = 12.5 mg/kg bw/day<br>Numerous effects                                             | 100                            |
| Long-term inhalation <sup>3</sup>                    | Rat chronic toxicity/carcinogenicity study                                      | NOAEL = 1.2 mg/kg bw/day<br>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<br>Reduced motor and locomotor activity                               | 100                            |
| Pick-your-own and residential dermal                 | Rat 28 day dermal toxicity study                                                | NOAEL = 300 mg/kg bw/day<br>Clinical chemistry and liver effects                          | 100                            |
| Cancer                                               | <b>Q<sub>1</sub>*</b> set at $1.72 \times 10^{-2}$ (mg/kg bw/day) <sup>-1</sup> |                                                                                           |                                |

<sup>1</sup> 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

<sup>2</sup> Since an oral NOAEL was selected, a dermal absorption factor was used in a route-to-route extrapolation

<sup>3</sup> 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<br>ha |        | Unit Exposure<br>$\mu\text{g/kg a.i. handled}$ |            |          |
|-------------------------------------------------|----------------------------|--------|------------------------------------------------|------------|----------|
|                                                 | 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<br>kg a.i./ha | Dermal<br>Exposure<br>mg/kg bw/day | Inhalation<br>Exposure<br>mg/kg bw/day | Dermal<br>MOE <sup>a</sup> | Inhalation<br>MOE <sup>a</sup> |
|------------------------|-----------------------|----------------------------|------------------------------------|----------------------------------------|----------------------------|--------------------------------|
| 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<br>(tree nuts) | airblast              | 0.25                       | 0.0628                             | 0.000529                               | 4776                       | 23649                          |

<sup>a</sup> Target MOE = 100

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

| Crop                   | Application<br>Equipment | Maximum<br>Appln Rate<br>kg a.i./ha | Maximum<br>Number of<br>Apps/season | Dermal<br>Exposure<br>mg/kg bw/day | Inhalation<br>Exposure<br>mg/kg bw/day | LADD<br>mg/kg bw/day | Cancer<br>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<br>farmer     | 0.15                                | 2                                   | 0.000757                           | 0.000329                               | 3.17E-06             | 5.46E-08       |
|                        | groundboom<br>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<br>farmer     | 0.15                                | 2                                   | 0.000757                           | 0.000329                               | 3.17E-06             | 5.46E-08       |
|                        | groundboom<br>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<br>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<br>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 <sup>2</sup> /h | DFR Value µg/cm <sup>2</sup> | Dermal Exposure mg/kg bw/day | Dermal MOE <sup>a</sup> |
|---------------------|------------------------------------------------------------------------|-------------------------------|---------------------------|-----------------------------------------|------------------------------|------------------------------|-------------------------|
| 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                   |

<sup>a</sup> 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 µg/cm <sup>2</sup> | 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:<br>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:<br>Level 2 (Dugout only) | Crops to be treated                                     | 1) grapes<br>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<br>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 (20 <sup>th</sup> percentile of five $K_{oc}$ values for fluopyram)                                                                                                                                                                                                 |
|                                                   | Aerobic soil biotransformation half-life (days)         | 654 for Level 1 and Level 2 (80 <sup>th</sup> percentile of half-life values; values for the two labels were averaged)<br>533 at Level 2 restricted application (80 <sup>th</sup> 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 ( $\mu\text{g a.i./L}$ ) |                     | Surface Water EEC ( $\mu\text{g a.i./L}$ ) |                     |                    |                     |
|--------------------|------------------------------------------|---------------------|--------------------------------------------|---------------------|--------------------|---------------------|
|                    | Daily <sup>1</sup>                       | Yearly <sup>2</sup> | Reservoir                                  |                     | Dugout             |                     |
|                    |                                          |                     | Daily <sup>3</sup>                         | Yearly <sup>4</sup> | Daily <sup>3</sup> | Yearly <sup>4</sup> |
| 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 90<sup>th</sup> percentile of daily average concentrations
- 2 90<sup>th</sup> percentile of yearly average concentrations
- 3 90<sup>th</sup> percentile of yearly peak concentrations
- 4 90<sup>th</sup> 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<br>( $\mu\text{g a.i./L}$ ) |                     | Surface Water EEC ( $\mu\text{g a.i./L}$ ) |                     |                    |                     |
|------------------------|---------------------------------------------|---------------------|--------------------------------------------|---------------------|--------------------|---------------------|
|                        | Daily <sup>3</sup>                          | Yearly <sup>4</sup> | Reservoir                                  |                     | Dugout             |                     |
|                        |                                             |                     | Daily <sup>1</sup>                         | Yearly <sup>2</sup> | Daily <sup>1</sup> | Yearly <sup>2</sup> |
| 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 90<sup>th</sup> percentile of yearly peak concentrations,  
 2 90<sup>th</sup> percentile of yearly average concentrations  
 3 90<sup>th</sup> percentile of maximum daily concentration for each of twelve starting years  
 4 90<sup>th</sup> 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 90<sup>th</sup> percentile of yearly averages calculated for these restricted years

**Table 15 Groundwater EECs ( $\mu\text{g/L}$ ) 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 |
|---------------------------------------|----------|-----------|-----------|-----------|----------|----------|----------|----------|----------|----------|----------|
| <b>Highest daily EEC</b>              |          |           |           |           |          |          |          |          |          |          |          |
| 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     |
| <b>Highest one year average value</b> |          |           |           |           |          |          |          |          |          |          |          |
| 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     |
| <b>Five year average EEC</b>          |          |           |           |           |          |          |          |          |          |          |          |
| 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     |
| <b>Ten year average EEC</b>           |          |           |           |           |          |          |          |          |          |          |          |
| 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       |
| <b>Twenty year average EEC</b>        |          |           |           |           |          |          |          |          |          |          |          |
| 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      |
| <b>Seventy year average EEC</b>       |          |           |           |           |          |          |          |          |          |          |          |
| 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_irr | 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]                                                                                                                      | [pyridyl-14C] |
|                                 |                                                                                                                                            | TRRs (ppm)                                                                                                                        | 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<br>AE C656948-7-hydroxy                                                                                      |               |
| Leaves                          | Fluopyram                                                                                                                                  | AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                                       |               |
| [pyridyl-14C]                   |                                                                                                                                            |                                                                                                                                   |               |
| Summer Cut                      | Fluopyram                                                                                                                                  | AE C656948-pyridyl-carboxylic acid<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy |               |
| Grapes                          | Fluopyram                                                                                                                                  | AE C656948-pyridyl-carboxylic acid<br>AE C656948-7-hydroxy                                                                        |               |

|                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                            |                                                                                                                                   |                                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------|
| Leaves                                                                                                                                                                                                                                                                                                                                                                                                     | Fluopyram                                                                                                                                  | AE C656948-pyridyl-carboxylic acid<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>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:<br>Hydroxylation of fluopyram leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy<br>Conjugation of AE C656948-7-hydroxy<br>Cleavage of hydroxylated active substance leading to AE C656948-benzamide and AE C656948-carboxylic acid |                                                                                                                                            |                                                                                                                                   |                                      |
| <b>Nature of the Residue in Potatoes</b>                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                            | <b>PMRA# 1599781 and 1599789</b>                                                                                                  |                                      |
| 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                                                                                                                                    |                                                                                                                                   |                                      |
| <b>Matrix</b>                                                                                                                                                                                                                                                                                                                                                                                              | <b>PHI (days)</b>                                                                                                                          | <b>[phenyl-14C] TRRs (ppm)</b>                                                                                                    | <b>[pyridyl-14C] TRRs (ppm)</b>      |
| 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<br>AE C656948-7-hydroxy                                                                                      |                                      |
| Potato leaves                                                                                                                                                                                                                                                                                                                                                                                              | Fluopyram                                                                                                                                  | AE C656948-benzamide<br>AE C656948-7-hydroxy                                                                                      |                                      |
| [pyridyl-14C]                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                            |                                                                                                                                   |                                      |
| Potato tuber                                                                                                                                                                                                                                                                                                                                                                                               | Fluopyram<br>AE C656948-pyridyl-carboxylic acid<br>(49.8% of the TRRs; 0.006 ppm)                                                          | AE C656948-pyridyl-carboxylic acid<br>AE C656948-7-hydroxy                                                                        |                                      |
| Potato leaves                                                                                                                                                                                                                                                                                                                                                                                              | Fluopyram                                                                                                                                  | AE C656948-pyridyl-carboxylic acid<br>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.                                                                                                                                                                                                                       |                                                                                                                                            |                                                                                                                                   |                                      |
| <b>Nature of the Residue in Beans</b>                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                            | <b>PMRA # 1599779 and 1599787</b>                                                                                                 |                                      |
| 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                                                                                     |                                                                                                                                   |                                      |
| <b>Matrix</b>                                                                                                                                                                                                                                                                                                                                                                                              | <b>PHI (days)</b>                                                                                                                          | <b>[phenyl-14C] TRRs (ppm)</b>                                                                                                    | <b>[pyridyl-14C] TRRs (ppm)</b>      |
| 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<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy             |
| Succulent beans                                                                                                                                                                                                                                                                                                                                                                                                          | Fluopyram<br>AE C656948-benzamide<br>(51.9% of the TRRs; 0.036 ppm)                                                                                | AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                                     |
| Dry beans                                                                                                                                                                                                                                                                                                                                                                                                                | Fluopyram<br>AE C656948-benzamide<br>(64.0% of the TRRs; 0.077 ppm)                                                                                | AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                                     |
| Straw                                                                                                                                                                                                                                                                                                                                                                                                                    | Fluopyram                                                                                                                                          | AE C656948-benzamide<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy             |
| [pyridyl-14C]                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                    |                                                                                                                                 |
| Green bean                                                                                                                                                                                                                                                                                                                                                                                                               | Fluopyram                                                                                                                                          | None                                                                                                                            |
| Foliage                                                                                                                                                                                                                                                                                                                                                                                                                  | Fluopyram                                                                                                                                          | AE C656948-PCA<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                   |
| Succulent beans                                                                                                                                                                                                                                                                                                                                                                                                          | AE C656948-PAA<br>(29.5% of the TRRs; 0.051 ppm)<br>AE C656948-PCA<br>(31.0% of the TRRs; 0.054 ppm)                                               | Fluopyram<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                        |
| Dry beans                                                                                                                                                                                                                                                                                                                                                                                                                | AE C656948-PAA<br>(22.6% of the TRRs; 0.070 ppm)<br>AE C656948-PCA<br>(32.5% of the TRRs; 0.100 ppm)                                               | Fluopyram<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                        |
| Straw                                                                                                                                                                                                                                                                                                                                                                                                                    | Fluopyram                                                                                                                                          | AE C656948-PCA<br>AE C656948-PAA<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy |
| The main reactions of fluopyram metabolism in the beans are:<br>Hydroxylation of fluopyram leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy<br>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<br>Cleavage of hydroxylated active substance leading to AE C656948-benzamide and AE C656948-carboxylic acid |                                                                                                                                                    |                                                                                                                                 |
| <b>Nature of the Residue in Red Bell Peppers</b>                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                    | <b>PMRA# 1599782 and 1599790</b>                                                                                                |
| 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)<br>Mature peppers (1x experiment, both radiolabels, three time points ranging from 55 to 96 days)<br>Mature peppers (4x experiment, pyridyl radiolabel only, three time points ranging from 55 to 96 days)<br>Rest of plant (1x experiment, 97 days) |                                                                                                                                                                                          |                      |
| <b>Matrix</b>            | <b>PHI (days)</b>                                                                                                                                                                                                                                                                                | <b>[phenyl-14C]</b>                                                                                                                                                                      | <b>[pyridyl-14C]</b> |
|                          |                                                                                                                                                                                                                                                                                                  | <b>TRRs (ppm)</b>                                                                                                                                                                        | <b>TRRs (ppm)</b>    |
| 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)                                                                                                                                                     |                      |
| <b>[phenyl-14C]</b>      |                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                          |                      |
| Intermediate plant       | Fluopyram                                                                                                                                                                                                                                                                                        | AE C656948-benzamide<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                                                                      |                      |
| Mature peppers (1x)      | Fluopyram                                                                                                                                                                                                                                                                                        | AE C656948-benzamide<br>AE C656948-7-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy                                                                                              |                      |
| Rest of plant            | Fluopyram<br>AE C656948-benzamide<br>(10.1% of the TRRs; 0.36 ppm)                                                                                                                                                                                                                               | AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside and malonic acid conjugates of AE C656948-7-hydroxy                                                                            |                      |
| <b>[pyridyl-14C]</b>     |                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                          |                      |
| Intermediate plant       | Fluopyram                                                                                                                                                                                                                                                                                        | AE C656948-PCA<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy<br>glucoside conjugate of AE C656948-7-hydroxy<br>di-glucoside conjugate of AE C656948-hydroxyethyl<br>AE C656948-N-oxide |                      |
| Mature peppers (4x)      | Fluopyram<br>AE C656948-PCA<br>(19.5% of the TRRs; 0.029 ppm)<br>AE C656948-PAA-glycoside<br>[12.5% (isomer 1) and 19.7% (isomer 2) of the TRRs; 0.019 and 0.029 ppm]                                                                                                                            | AE C656948-PAA<br>AE C656948-7-hydroxy                                                                                                                                                   |                      |
| Mature peppers (1x)      | Fluopyram<br>AE C656948-PCA<br>(43.5% of the TRRs; 0.026 ppm)<br>AE C656948-PAA-glycoside<br>[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<br>glucoside conjugate of AE C656948-7-hydroxy<br>di-glucoside conjugate of AE C656948-hydroxyethyl<br>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.

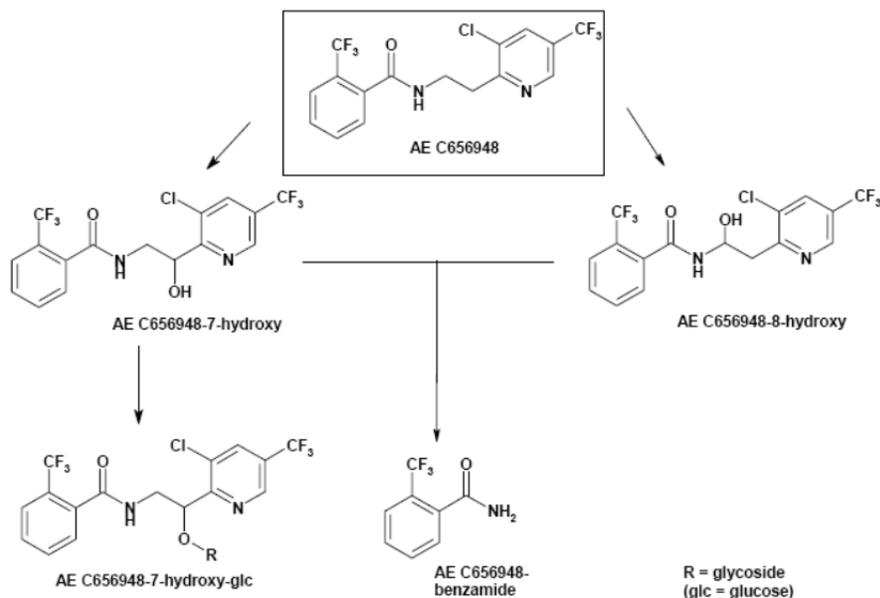
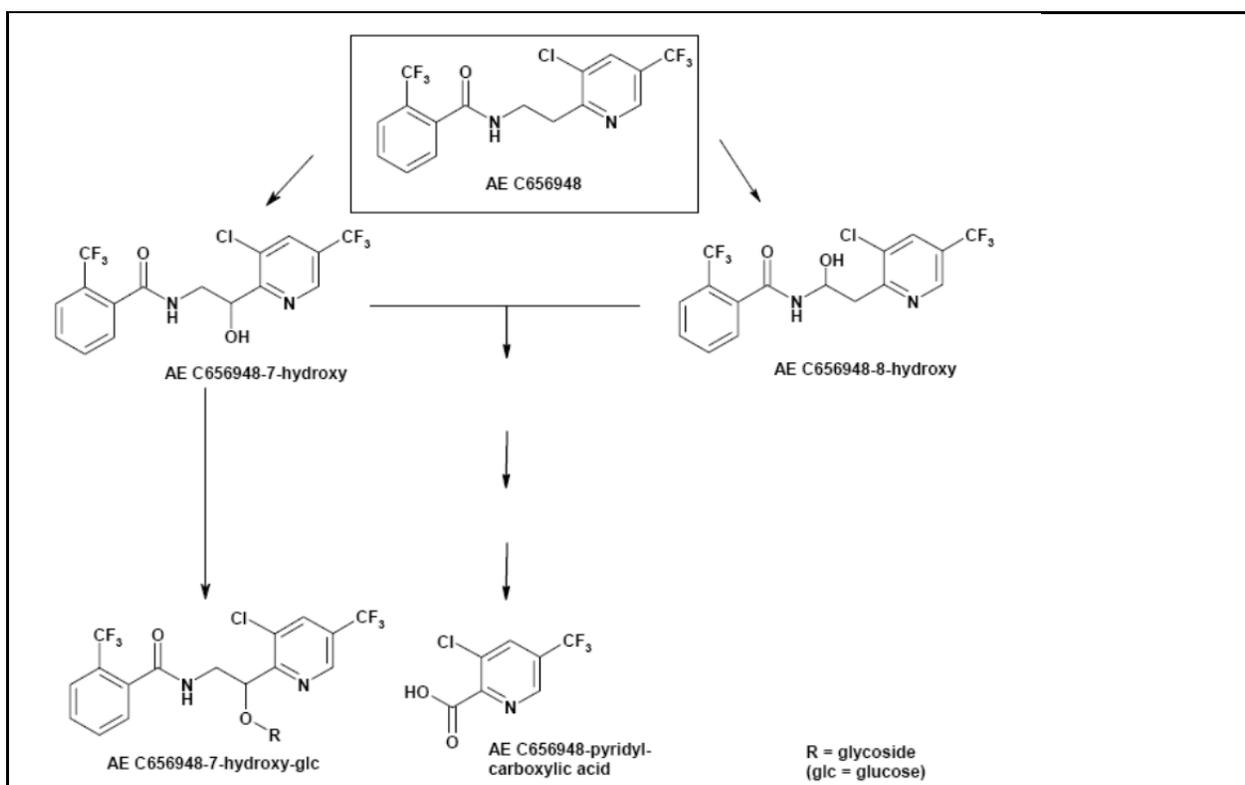
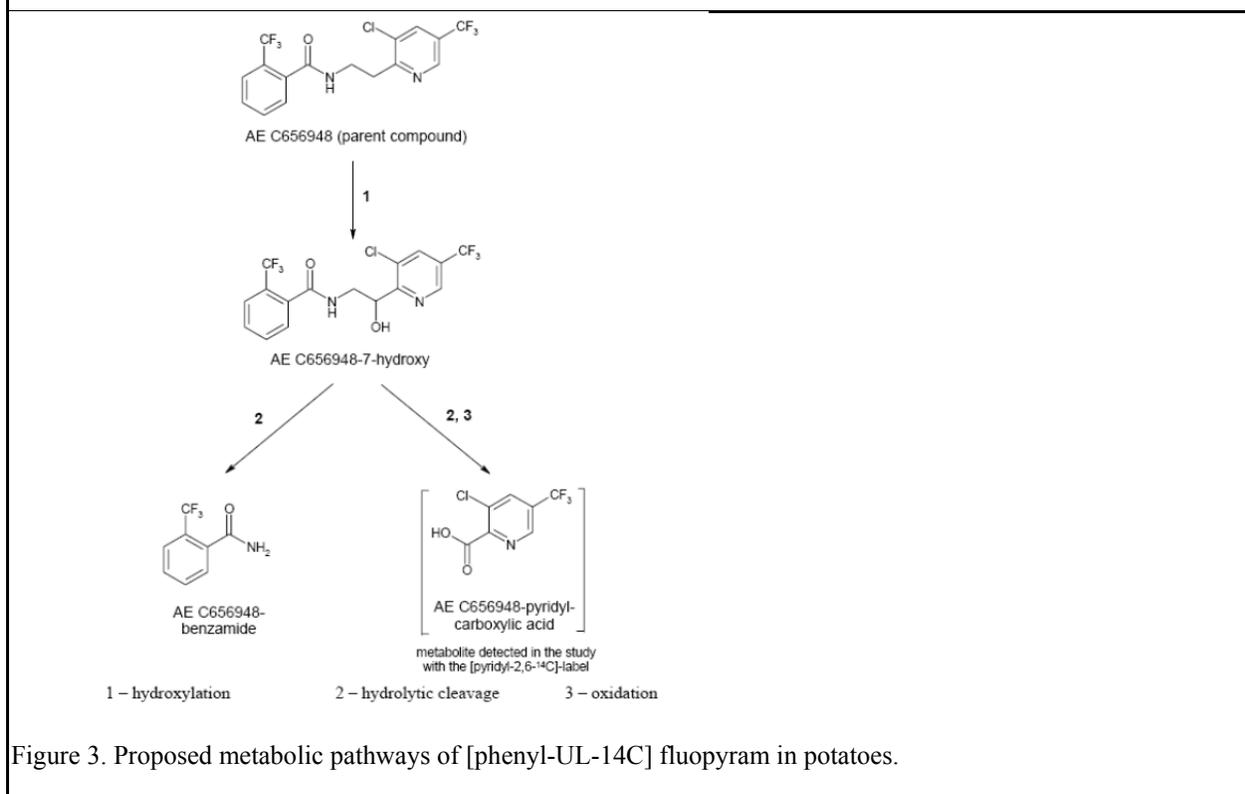


Figure 1. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in grapes.

Figure 2. Proposed metabolic pathways of [pyridyl-2,6-<sup>14</sup>C] fluopyram in grapes.Figure 3. Proposed metabolic pathways of [phenyl-UL-<sup>14</sup>C] fluopyram in potatoes.

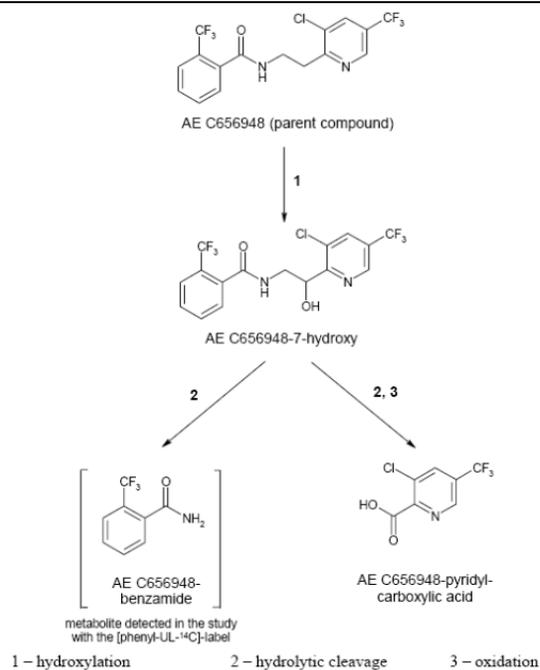


Figure 4. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in potatoes.

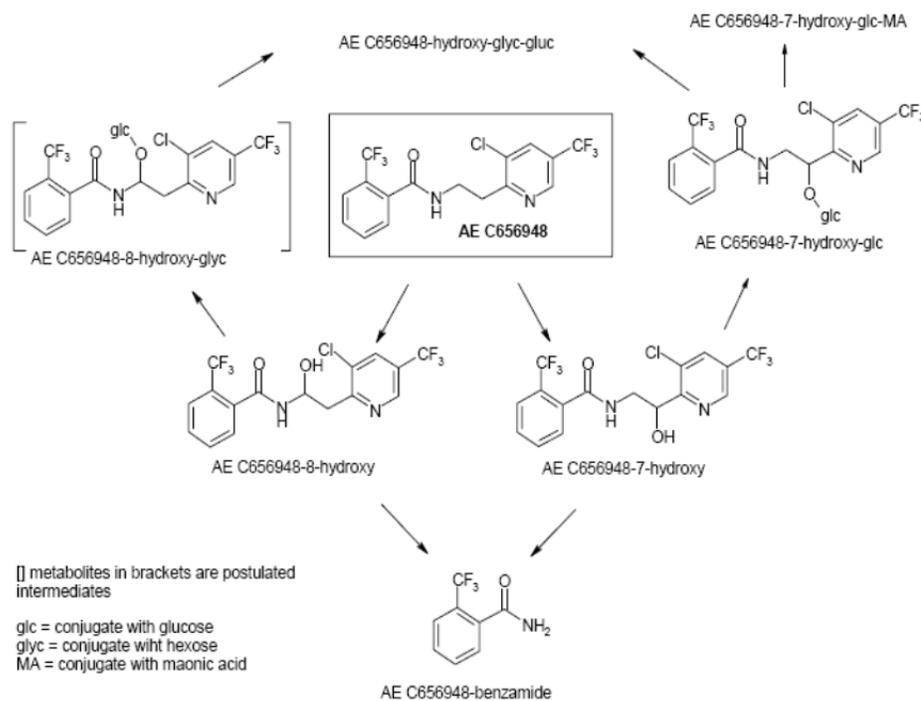


Figure 5. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in beans.

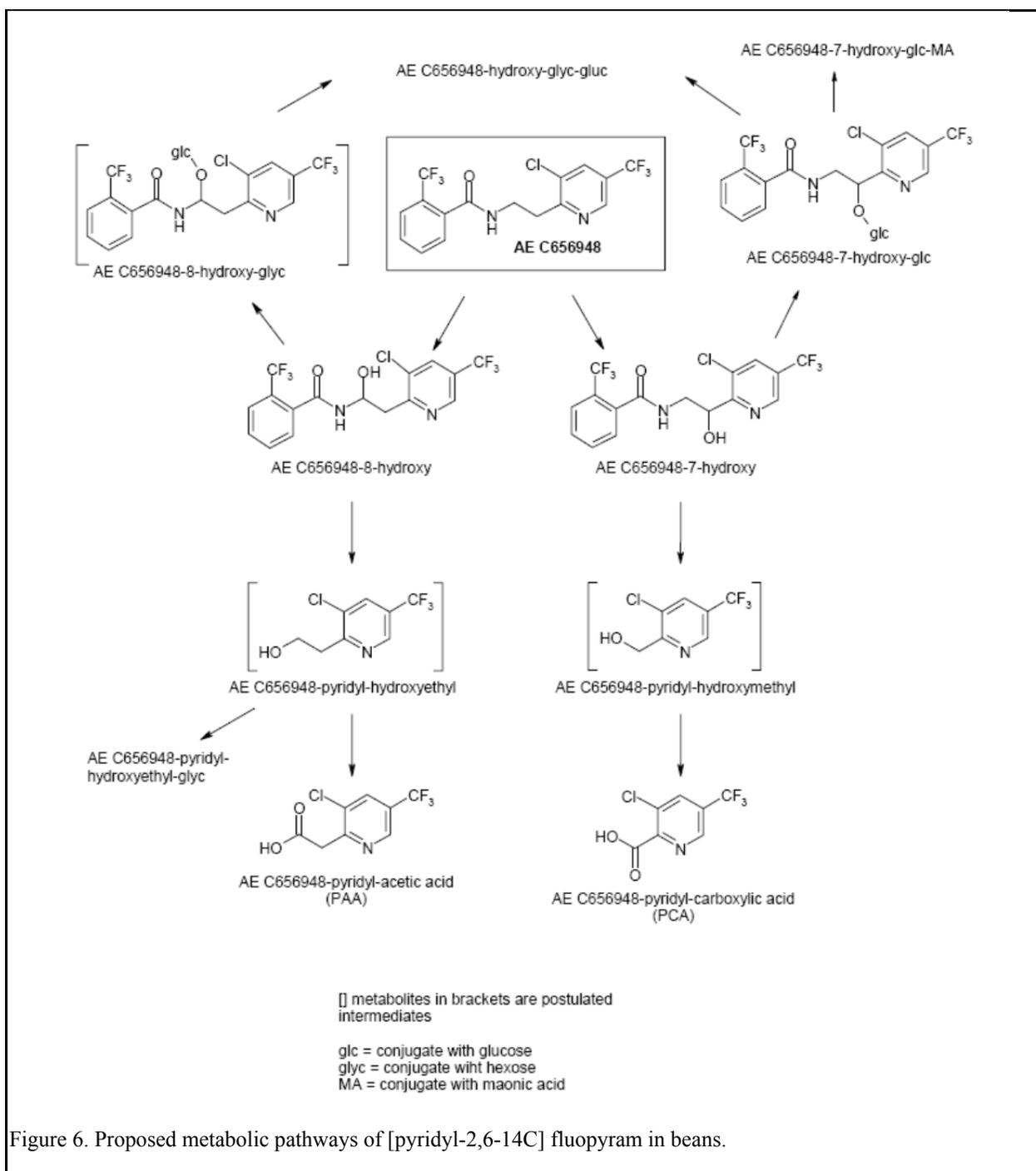
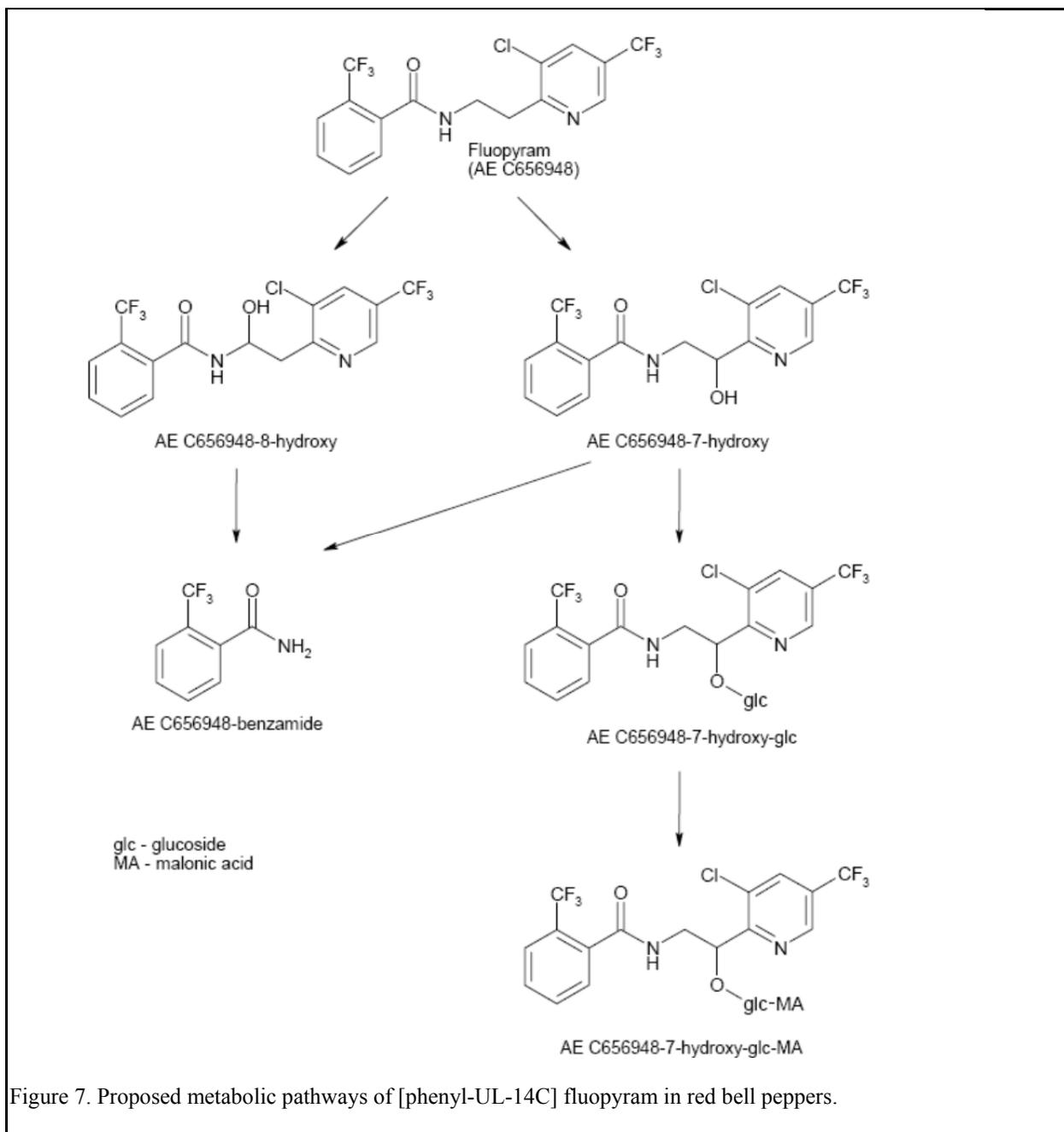


Figure 6. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in beans.



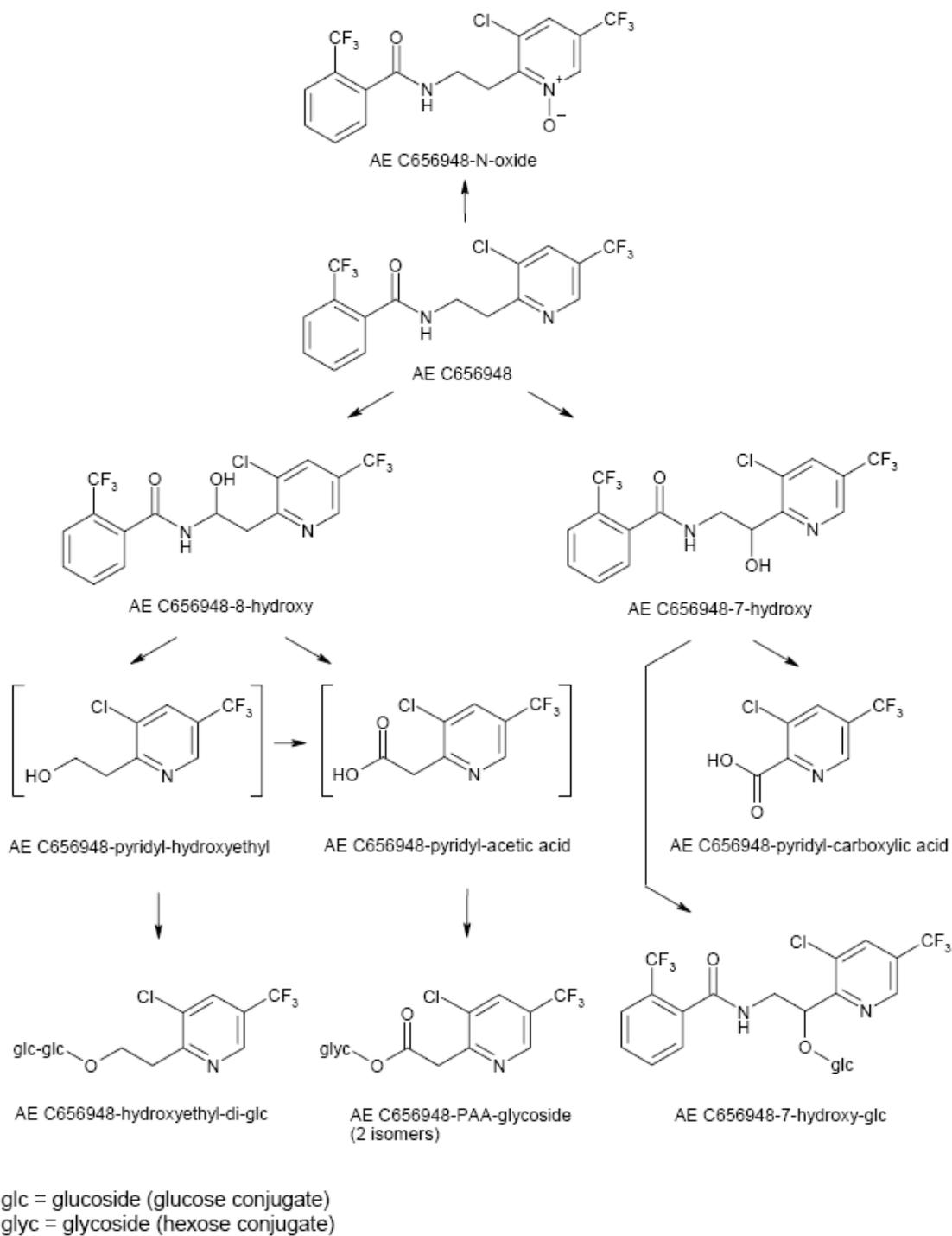


Figure 8. Proposed metabolic pathways of [pyridyl-2,6-14C] fluopyram in red bell peppers.

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

| <b>Confined Accumulation in Rotational Crops – Wheat, Swiss chard, turnip</b> |                                                                                                                          | <b>PMRA# 1599780 and 1599788</b>       |                                                                                                                                                                                                        |
|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 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                                                        |                                                                                                                          |                                        |                                                                                                                                                                                                        |
| <b>Matrix</b>                                                                 | <b>PBI (days)</b>                                                                                                        | <b>Major Metabolites (&gt;10% TRR)</b> | <b>Minor Metabolites (&lt;10% TRR)</b>                                                                                                                                                                 |
| Phenyl-UL-C14                                                                 |                                                                                                                          |                                        |                                                                                                                                                                                                        |
| Wheat forage                                                                  | 30                                                                                                                       | Fluopyram                              | AE C656948-benzoic acid<br>AE C656948-benzamide<br>AE C656948-7-hydroxy-glc-MA (isomer 1)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy   |
|                                                                               | 139                                                                                                                      | Fluopyram                              | AE C656948-benzoic acid<br>AE C656948-benzamide<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy |
|                                                                               | 280                                                                                                                      | Fluopyram                              | AE C656948-benzamide<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy                            |
| Wheat hay                                                                     | 30                                                                                                                       | Fluopyram                              | AE C656948-benzoic acid<br>AE C656948-benzamide<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy |
|                                                                               | 139                                                                                                                      | Fluopyram                              | AE C656948-benzoic acid<br>AE C656948-benzamide<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy |
|                                                                               | 280                                                                                                                      | Fluopyram<br>AE C656948-7-hydroxy      | AE C656948-benzamide<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-8-hydroxy                                                    |

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

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

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |     |                                                                                |                                                                                                                                                                                  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|--------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 280 | Fluopyram<br>AE C656948-7-hydroxy                                              | AE C656948-methyl-sulfoxide<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-8-hydroxy-glc-MA<br>AE C656948-7-hydroxy-glc<br>AE C656948-8-hydroxy                       |
| Wheat grain                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 30  | Fluopyram<br>AE C656948- pyridyl carboxylic acid                               | AE C656948-methyl-sulfoxide<br>AE C656948-7-hydroxy                                                                                                                              |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 139 | Fluopyram<br>AE C656948-methyl-sulfoxide<br>AE C656948-pyridyl carboxylic acid | AE C656948-7-hydroxy                                                                                                                                                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 280 | Fluopyram<br>AE C656948-methyl-sulfoxide<br>AE C656948-pyridyl carboxylic acid | AE C656948-7-hydroxy                                                                                                                                                             |
| Swiss chard                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 30  | Fluopyram<br>AE C656948-7-hydroxy                                              | AE C656948-methyl-sulfoxide<br>AE C656948-pyridyl carboxylic acid<br>AE C656948-7-OH-SA<br>AE C656948-7-hydroxy-glc<br>AE C656948-8-hydroxy                                      |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 139 | Fluopyram<br>AE C656948-7-OH-SA<br>AE C656948-7-hydroxy                        | AE C656948-methyl-sulfoxide<br>AE C656948-pyridyl carboxylic acid<br>AE C656948-7-hydroxy-glc<br>AE C656948-8-hydroxy                                                            |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 280 | Fluopyram<br>AE C656948-7-OH-SA<br>AE C656948-7-hydroxy                        | AE C656948-methyl-sulfoxide<br>AE C656948-pyridyl carboxylic acid<br>AE C656948-7-hydroxy-glc<br>AE C656948-8-hydroxy                                                            |
| Turnip tops<br>(leaves)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 30  | Fluopyram<br>AE C656948-phenol-glc                                             | AE C656948-pyridyl carboxylic acid<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-7-OH-SA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 139 | Fluopyram<br>AE C656948-phenol-glc                                             | AE C656948-pyridyl carboxylic acid<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-7-OH-SA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 280 | Fluopyram<br>AE C656948-phenol-glc                                             | AE C656948-pyridyl carboxylic acid<br>AE C656948-7-hydroxy-glc-MA (isomer 1&2)<br>AE C656948-7-OH-SA<br>AE C656948-7-hydroxy-glc<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy |
| Turnip roots                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 30  | Fluopyram                                                                      | AE C656948-pyridyl carboxylic acid<br>AE C656948-7-hydroxy<br>AE C656948-8-hydroxy                                                                                               |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 139 | Fluopyram                                                                      | AE C656948-7-hydroxy                                                                                                                                                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 280 | Fluopyram                                                                      | AE C656948-7-hydroxy                                                                                                                                                             |
| <p>Proposed Metabolism in Rotational Crops</p> <p>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.</p> |     |                                                                                |                                                                                                                                                                                  |

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.

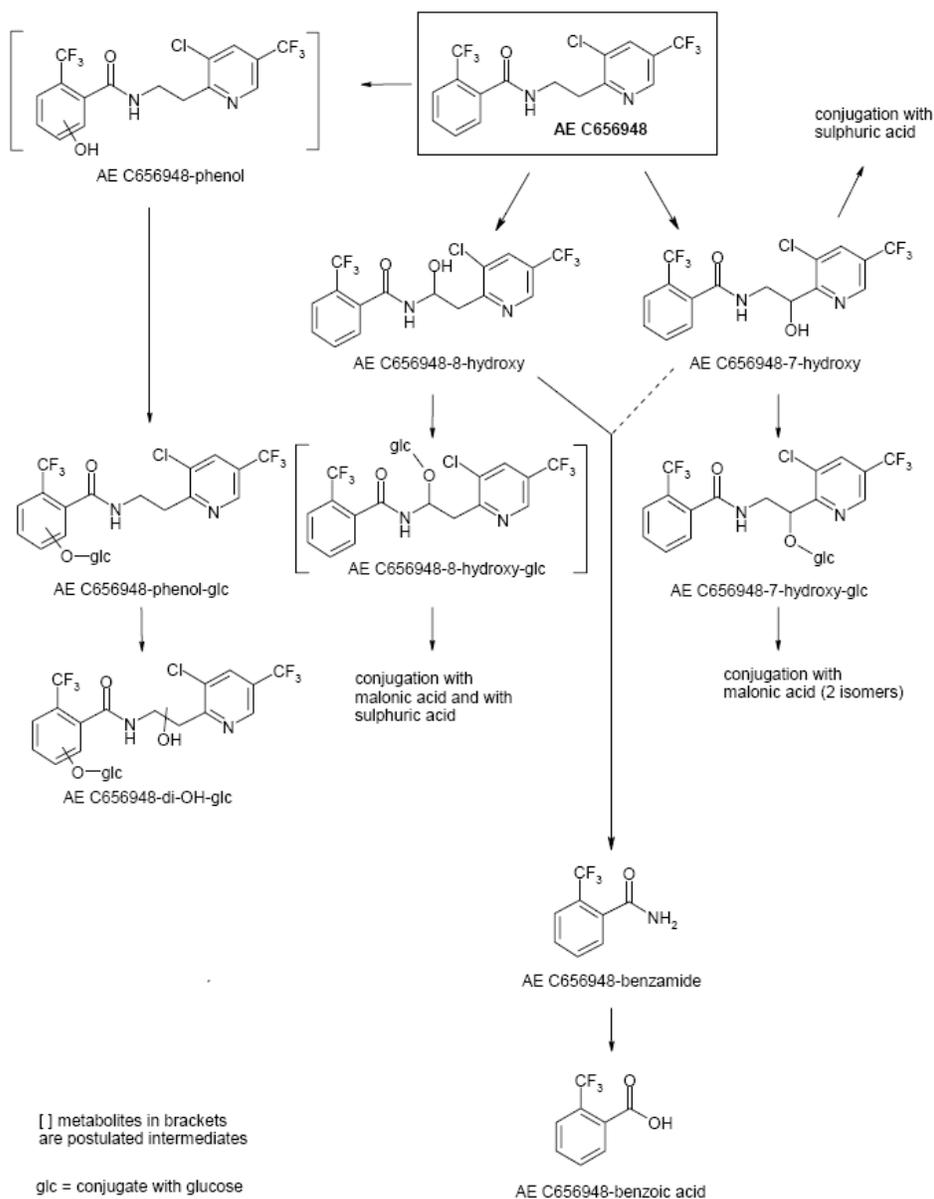


Figure 9. Proposed metabolic pathways of [phenyl-UL-14C] fluopyram in rotational crops.



**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- <sup>14</sup> 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- <sup>14</sup> C]fluopyram. Animals were sacrificed about 24h after the last dose. |                                              |                                     |                                                   |                                                                |
| <i>Phenyl Radiolabel:</i> 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.                                                                                              |                                              |                                     |                                                   |                                                                |
| <i>Pyridyl Radiolabel:</i> 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- <sup>14</sup> C]fluopyram. The metabolism of fluopyram in hens is well understood.                                                                                                                                                                                                                                                                           |                                              |                                     |                                                   |                                                                |
| Matrices                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | % of Administered Dose                       |                                     |                                                   |                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | [phenyl- <sup>14</sup> C]                    |                                     | [pyridyl- <sup>14</sup> C]                        |                                                                |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | TRRs (ppm)<br>(mean of 6 hens)               | % of Administered<br>Dose           | TRRs (ppm)<br>(mean of 6 hens)                    | % of Administered<br>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- <sup>14</sup> C]                    | [pyridyl- <sup>14</sup> C]          | [phenyl- <sup>14</sup> C]                         | [pyridyl- <sup>14</sup> C]                                     |
| Eggs                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | AE C656948-benzamide                         | Fluopyram<br>AE C656948-Z-olefine   | Fluopyram<br>AE C656948-Z-olefine                 | AE C656948-E-olefine<br>AE C656948-PAA<br>AE C656948-7-hydroxy |
| Muscle                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | AE C656948-benzamide                         | AE C656948-Z-olefine                | AE C656948-Z-olefine                              | Fluopyram<br>AE C656948-E-olefine                              |
| Fat                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | AE C656948-benzamide<br>AE C656948-Z-olefine | Fluopyram<br>AE C656948-Z/E-olefine | Fluopyram<br>AE C656948-E-olefine                 | None                                                           |
| Liver                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | AE C656948-benzamide                         | AE C656948-E-olefine                | AE C656948-Z/E-olefine<br>AE C656948-benzoic acid | AE C656948-Z-olefine<br>AE C656948-PAA<br>AE C656948-7-hydroxy |

| <b>Nature of the Residue in Lactating Goat</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                             | <b>PMRA # 1599783 and 1599791</b> |                            |         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------------------|----------------------------|---------|
| <p>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-<sup>14</sup>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-<sup>14</sup>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.</p> <p><i>Phenyl Radiolabel:</i> 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.</p> <p>The metabolic reactions of [phenyl-UL-<sup>14</sup>C]fluopyram detected in the lactating goat were:</p> <ul style="list-style-type: none"> <li>• hydroxylation of the ethylene bridge of the molecule resulting in AE C656948-7-hydroxy, AE C656948-8-hydroxy, and a dihydroxylated compound,</li> <li>• hydroxylation of the phenyl ring leading to AE C656948-phenol,</li> <li>• conjugation of the hydroxylated metabolites with glucuronic acid,</li> <li>• 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,</li> <li>• cleavage of the aliphatic chain to form AE C656948-benzamide,</li> <li>• hydroxylation of AE C656948-benzamide followed by conjugation with sulphate.</li> </ul> <p><i>Pyridyl Radiolabel:</i> 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.</p> <p>The metabolic reactions of [pyridyl-2,6-<sup>14</sup>C]fluopyram detected in the lactating goat were:</p> <ul style="list-style-type: none"> <li>• hydroxylation of the ethylene bridge of the molecule resulting in AE C656948-7-hydroxy, AE C656948-8-hydroxy, and a dihydroxylated compound,</li> <li>• hydroxylation of the phenyl ring leading to AE C656948-phenol,</li> <li>• conjugation of the hydroxylated metabolites with glucuronic acid,</li> <li>• 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),</li> <li>• molecular cleavage to AE C656948-pyridyl-hydroxyethyl followed by conjugation with glucuronic acid,</li> <li>• oxidation of AE C656948-pyridyl-hydroxyethyl to AE C656948-pyridyl-acetic acid.</li> </ul> <p>The results are in very good agreement with the results from the lactating goat metabolism study with [phenyl-UL-<sup>14</sup>C] fluopyram. The metabolism of fluopyram in goats is well understood.</p> |                             |                                   |                            |         |
| Matrices                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | % of Administered Dose (AD) |                                   |                            |         |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | [phenyl- <sup>14</sup> C]   |                                   | [pyridyl- <sup>14</sup> 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- <sup>14</sup> C]                                 | [pyridyl- <sup>14</sup> C]                                                                                                                                 | [phenyl- <sup>14</sup> C]                                                                                                                                         |
| Milk                   | AE C656948-benzamide                                      | Fluopyram<br>AE C656948-Z-olefine<br>AE C656948-7-hydroxy | Fluopyram<br>AE C656948-Z-olefine<br>AE C656948-7-hydroxy<br>AE C656948-7-OH-GA<br>AE C656948-benzamide-SA                                                 | AE C656948-7-OH-GA<br>AE C656948-8-OH-GA<br>AE C656948-E-olefine                                                                                                  |
| Muscle                 | AE C656948-benzamide                                      | Fluopyram<br>AE C656948-Z-olefine<br>AE C656948-7-hydroxy | AE C656948-7-hydroxy<br>AE C656948-7-OH-GA<br>AE C656948-benzamide-SA                                                                                      | AE C656948-7-OH-GA<br>AE C656948-8-OH-GA<br>AE C656948-E-olefine                                                                                                  |
| Fat                    | Fluopyram<br>AE C656948-benzamide<br>AE C656948-Z-olefine | Fluopyram<br>AE C656948-Z-olefine<br>AE C656948-7-hydroxy | AE C656948-E-olefine<br>AE C656948-7-hydroxy                                                                                                               | AE C656948-E-olefine                                                                                                                                              |
| Liver                  | AE C656948-benzamide                                      | AE C656948-7-OH-GA                                        | Fluopyram<br>AE C656948-Z/E-olefine<br>AE C656948-7-hydroxy<br>AE C656948-7-OH-GA<br>AE C656948-8-OH-GA<br>AE C656948-benzamide-SA<br>AE C656948-phenol-GA | Fluopyram<br>AE C656948-phenol-GA<br>AE C656948-di-OH-GA<br>AE C656948-8-OH-GA<br>AE C656948-E-olefine<br>AE C656948-7-hydroxy                                    |
| Kidney                 | AE C656948-benzamide                                      | AE C656948-7-OH-GA                                        | Fluopyram<br>AE C656948-7-hydroxy<br>AE C656948-7-OH-GA<br>AE C656948-8-OH-GA<br>AE C656948-benzamide-SA<br>AE C656948-phenol-GA<br>AE C656948-di-OH-GA    | AE C656948-PAA<br>AE C656948-hydroxyethyl-GA<br>AE C656948-phenol-GA<br>AE C656948-di-OH-GA<br>AE C656948-8-OH-GA<br>AE C656948-E-olefine<br>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 ( $\leq 0.007$  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.}

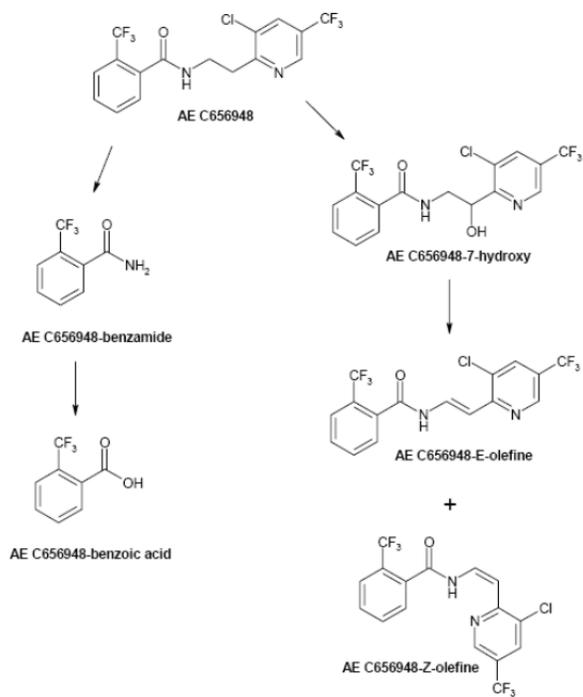


Figure 11. Proposed metabolic pathways of [phenyl-UL-<sup>14</sup>C] fluopyram in laying hen.

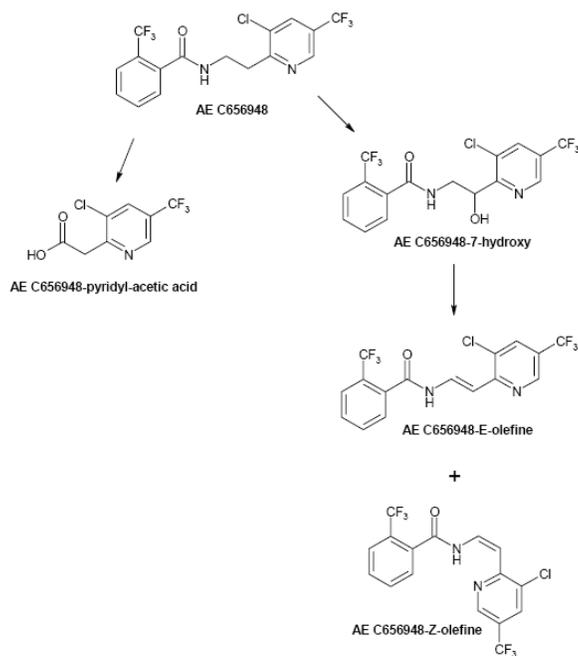


Figure 12. Proposed metabolic pathways of [pyridyl-2,6-<sup>14</sup>C] fluopyram in laying hen.

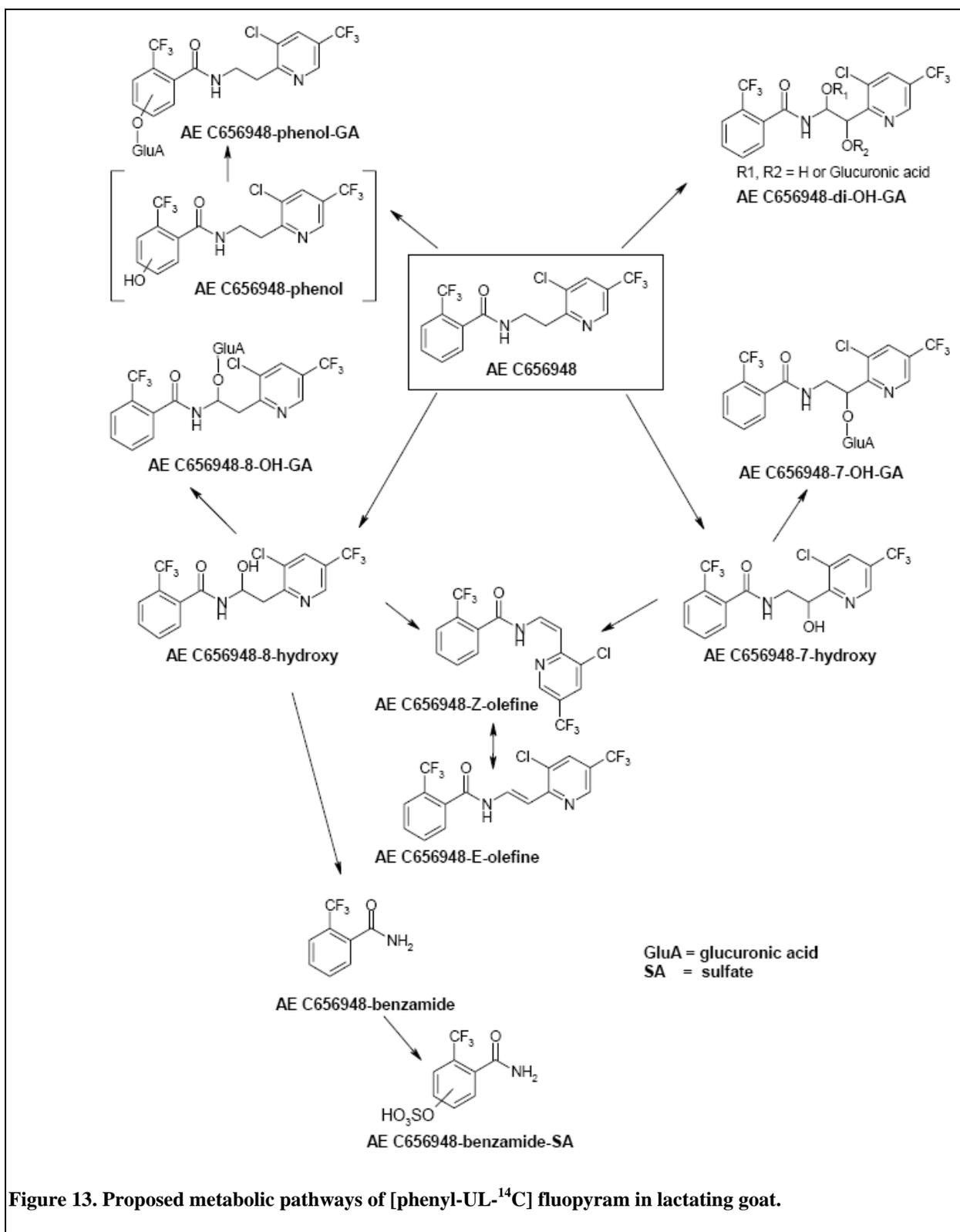


Figure 13. Proposed metabolic pathways of [phenyl-UL-<sup>14</sup>C] fluopyram in lactating goat.

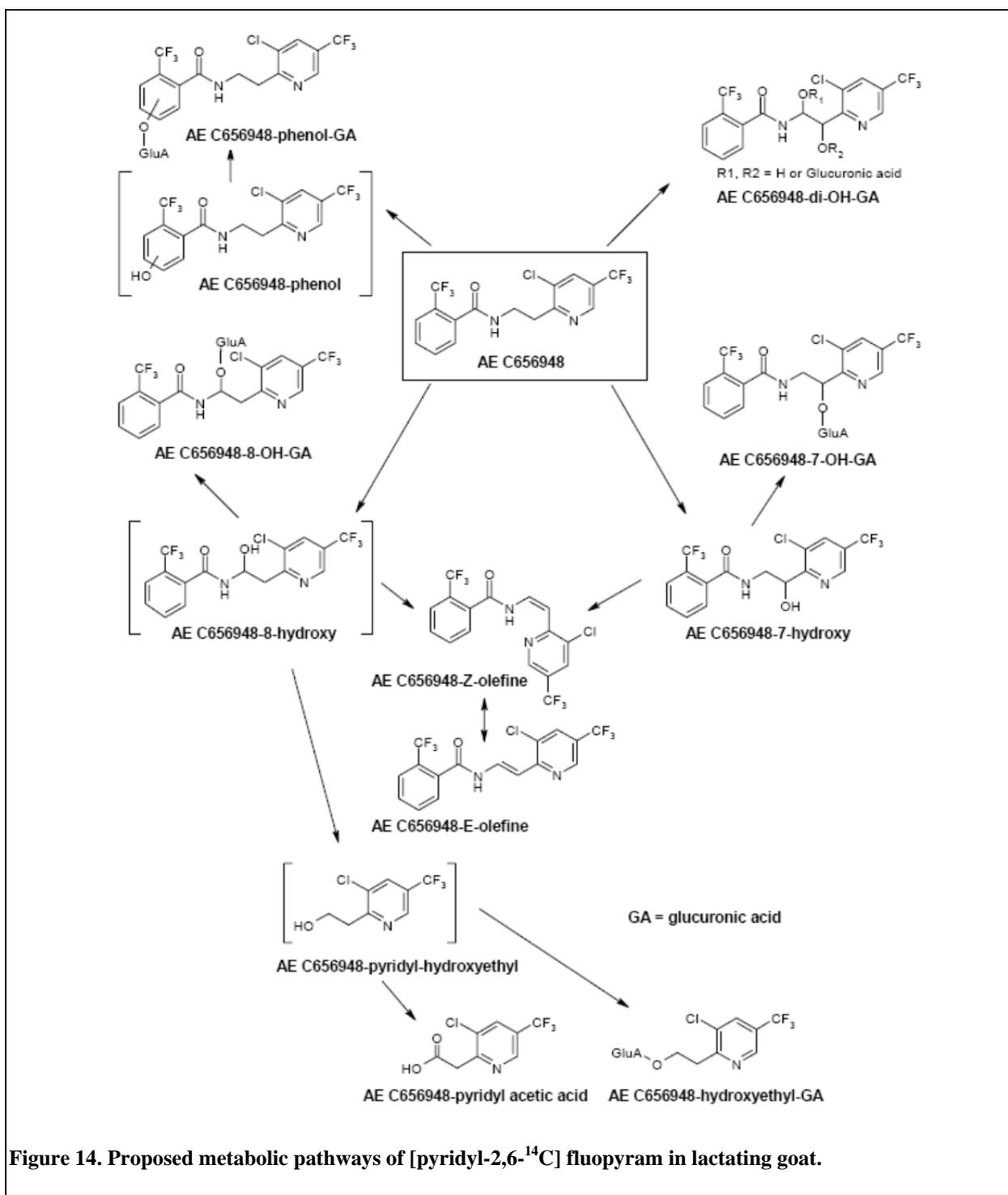


Figure 14. Proposed metabolic pathways of [pyridyl-2,6-<sup>14</sup>C] fluopyram in lactating goat.

**Table 18d Freezer Storage Stability**

| <b>Freezer Storage Stability</b>                                                                                                                                                                                                                                                                                   | <b>PMRA# 1599821, 1784472, 1983731, 1599801, 1804905, 1983732</b> |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| Residues of fluopyram and the metabolite fluopyram-benzamide are stable for up to 36 months at $\leq -18^{\circ}\text{C}$ in lettuce head, wheat grain, rape seed, dry pea seed and orange.                                                                                                                        |                                                                   |
| Stability of Other Metabolites:<br>Fluopyram-pyridyl-acetic acid: up to 36 months in/on lettuce head, wheat grain, rape seed and dry pea seed.<br>Fluopyram-pyridyl-carboxylic acid: up to 36 months in dry pea seed, rape seed and orange.<br>Fluopyram-7-hydroxy: up to 36 months in/on wheat grain and lettuce. |                                                                   |

**Table 18e Crop Field Trials and Residue Decline**

| <b>Crop Field Trials &amp; Residue Decline – Potatoes</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                              |            |                                |         |        |        | <b>PMRA# 1654363</b> |             |           |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------|--------------------------------|---------|--------|--------|----------------------|-------------|-----------|--|
| 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 ( $<0.01$ ppm) 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     |  |
| <b>Crop Field Trials &amp; Residue Decline – Sugar beets</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                              |            |                                |         |        |        | <b>PMRA# 1654364</b> |             |           |  |
| 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     |  |

| <b>Crop Field Trials &amp; Residue Decline – Dry beans and peas</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                              |            |                                |       |       | <b>PMRA# 1661215</b> |                |             |           |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------|--------------------------------|-------|-------|----------------------|----------------|-------------|-----------|
| <p>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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                              |            |                                |       |       |                      |                |             |           |
| <p>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.</p> |                              |            |                                |       |       |                      |                |             |           |
| <p>At the PHI of 13-14 days, residues of fluopyram ranged from &lt;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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                              |            |                                |       |       |                      |                |             |           |
| <p>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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                              |            |                                |       |       |                      |                |             |           |
| 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      |
| <b>Crop Field Trials &amp; Residue Decline – Melons</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                              |            |                                |       |       | <b>PMRA# 1661219</b> |                |             |           |
| <p>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.</p>                                                                                                                                                                                                                                                                                                                                |                              |            |                                |       |       |                      |                |             |           |
| <p>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.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                              |            |                                |       |       |                      |                |             |           |
| 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     |
| <b>Crop Field Trials &amp; Residue Decline – Apples</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                              |            |                                |       |       | <b>PMRA# 1670088</b> |                |             |           |
| <p>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.</p>             |                              |            |                                |       |       |                      |                |             |           |

| 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                      |                |              |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR)    | Mean<br>(STMR) | Std.<br>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        |
| <b>Crop Field Trials &amp; Residue Decline – Cherries</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                 |               |                                |       |       |       | <b>PMRA# 1661231</b> |                |              |
| 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                      |                |              |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR)    | Mean<br>(STMR) | Std.<br>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        |
| <b>Crop Field Trials &amp; Residue Decline – Grapes</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                 |               |                                |       |       |       | <b>PMRA# 1599586</b> |                |              |
| 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                      |                |              |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR)    | Mean<br>(STMR) | Std.<br>Dev. |
| Grapes                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 439 - 513                       | 6-7           | 32                             | 0.096 | 0.950 | 0.948 | 0.372                | 0.401          | 0.229        |
| <b>Crop Field Trials &amp; Residue Decline – Strawberries</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                 |               |                                |       |       |       | <b>PMRA# 1599587</b> |                |              |
| 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 to 0.045 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.

| <p>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.</p> <p>At the PHI of 7 days, residues of fluopyram ranged from &lt;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.</p>                                                                                                                     |                              |            |                                |       |       |       |                      |             |           |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|------------|--------------------------------|-------|-------|-------|----------------------|-------------|-----------|
| 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      |
| <b>Crop Field Trials &amp; Residue Decline – Bananas</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                              |            |                                |       |       |       | <b>PMRA# 1661260</b> |             |           |
| <p>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.</p> <p>Residues of fluopyram on bananas (bagged; PHI of 0 day) ranged from &lt;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 &lt;0.01 ppm and 0.13 ppm, respectively, at the 6-7 day PHI.</p> |                              |            |                                |       |       |       |                      |             |           |
| 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**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |  |                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|----------------------|
| <b>Residue Data in Rotational Crops – Limited Field Accumulation in Wheat, Turnip and Mustard Greens</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |  | <b>PMRA# 1661301</b> |
| <p>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.</p> <p>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 PHI 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.</p> <p>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 PHI 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.</p> <p>Rotated mustard greens: Two foliar spray applications of AE C656948 500 SC were made to cover crops at a rate of</p> |  |                      |

| 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 PHI 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     |
| <b>Residue Data in Rotational Crops - Alfalfa</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                              |            |                                |       |       |       | <b>PMRA# 1654401</b> |             |           |
| 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 PHI 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      |
| <b>Residue Data in Rotational Crops - Cotton</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                              |            |                                |       |       |       | <b>PMRA# 1661299</b> |             |           |
| 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 PHI 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.                                                                                                                                                                                                                                                                                                                                                   |                              |            |                                |       |       |       |                      |             |           |
| <b>Crop Field Trials Used as Rotational Crop Data – Field Corn and Sweet Corn</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                              |            |                                |       |       |       | <b>PMRA# 1661248</b> |             |           |
| 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                      |                |              |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|---------------|--------------------------------|-------|-------|-------|----------------------|----------------|--------------|--|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR)    | Mean<br>(STMR) | Std.<br>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            |  |
| <b>Crop Field Trials Used as Rotational Crop Data – Wheat and Sorghum</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                 |               |                                |       |       |       | <b>PMRA# 1661247</b> |                |              |  |
| 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                      |                |              |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR)    | Mean<br>(STMR) | Std.<br>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         |  |
| <b>Crop Field Trials Used As Rotational Crop Data – Canola</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                 |               |                                |       |       |       | <b>PMRA# 1661254</b> |                |              |  |
| 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                      |                |              |  |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR)    | Mean<br>(STMR) | Std.<br>Dev. |  |
| Canola seeds                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 500                             | 12-14         | 16                             | 0.089 | 3.00  | 2.89  | 0.140                | 0.512          | 0.934        |  |
| <b>Crop Field Trials Used As Rotational Crop Data – Soybeans</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                 |               |                                |       |       |       | <b>PMRA# 1661216</b> |                |              |  |
| 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 (trifoliolate 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<br>(g a.i./ha) | PHI<br>(days) | Fluopyram Residue Levels (ppm) |       |       |       |                   |                |              |
|----------------|---------------------------------|---------------|--------------------------------|-------|-------|-------|-------------------|----------------|--------------|
|                |                                 |               | n                              | Min   | Max   | HAFT  | Median<br>(STMdR) | Mean<br>(STMR) | Std.<br>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**

| <b>PROCESSED FOOD AND FEED - Potato</b>     |                                                                                  | <b>PMRA# 1654380 (or 1661287)</b>                      |
|---------------------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------|
| 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                                                                             |                                                        |
| <b>PROCESSED FOOD AND FEED – Sugar beet</b> |                                                                                  | <b>PMRA# 1654379 (or 1661286)</b>                      |
| 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                                                                             |                                                        |
| <b>PROCESSED FOOD AND FEED – Apple</b>      |                                                                                  | <b>PMRA# 1654383 (or 1661291), 1654393 and 1654394</b> |
| 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                                                                         |
| <b>PROCESSED FOOD AND FEED – Grape</b>             |                                                                              |
| <b>PMRA# 1599645, 1599646, 1599660 and 1599584</b> |                                                                              |
| 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                                                                         |
| <b>PROCESSED FOOD AND FEED – Strawberry</b>        |                                                                              |
| <b>PMRA# 1599587, 1599659 and 1599658</b>          |                                                                              |
| 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                                                                         |                                                        |
| <b>PROCESSED FOOD AND FEED - Peanut</b>     |                                                                              | <b>PMRA# 1654372 (or 1661275)</b>                      |
| 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                                                                         |                                                        |
| <b>PROCESSED FOOD AND FEED - Wheat</b>      |                                                                              | <b>PMRA# 1654374 (or 1661280)</b>                      |
| 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                                                                          |                                                        |
| <b>PROCESSED FOOD AND FEED - Field corn</b> |                                                                              | <b>PMRA# 1654373 (or 1661276)</b>                      |
| 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                                                                         |                                                        |
| <b>PROCESSED FOOD AND FEED - Canola</b>     |                                                                              | <b>PMRA# 1654378 (or 1661285), 1654391 and 1654395</b> |
| 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                                                                                                         |
| <b>PROCESSED FOOD AND FEED - Soybeans</b> |                                                                                                              |
| <b>PMRA# 1654375 (or 1661282)</b>         |                                                                                                              |
| 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                                                                                                         |
| <b>PROCESSED FOOD AND FEED - Cotton</b>   |                                                                                                              |
| <b>PMRA# 1654376 (or 1661283)</b>         |                                                                                                              |
| 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**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|
| <b>LIVESTOCK FEEDING – Dairy cattle</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>PMRA# 1599761</b> |
| <p>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.)</p> <p>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.</p> |                      |

| 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       |
| <b>Fluopyram</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                     |                             |                             |                            |
| Milk (Day 4 to end)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <0.01                                               | <0.01-0.02<br>(mean = 0.01) | 0.02-0.09<br>(mean = 0.03)  | 0.06-0.17<br>(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                       |
| <b>AE C656948-benzamide</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                     |                             |                             |                            |
| Milk (Day 8 to end)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 0.01-0.09<br>(mean = 0.02)                          | 0.15-0.37<br>(mean = 0.22)  | 0.40-0.77<br>(mean = 0.54)  | 1.1-1.9<br>(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                        |
| <b>Combined Residues of Fluopyram and AE C656948-benzamide</b>                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                     |                             |                             |                            |
| Milk (Day 8 to end)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <0.02-<0.10<br>(mean = 0.03)                        | <0.16-0.39<br>(mean = 0.23) | 0.42-0.80<br>(mean = 0.57)  | 1.2-2.0<br>(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                        |
| <b>AE C656948-olefines</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                     |                             |                             |                            |
| Milk (Day 8 to end)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | <0.02                                               | ≤0.02                       | <0.02-0.05<br>(mean = 0.02) | 0.07-0.14<br>(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                       |
| <b>LIVESTOCK FEEDING – Laying Hen</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                     |                             | <b>PMRA# 1599760</b>        |                            |
| 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<br>(mean = 0.08)   | 0.20-0.23<br>(mean = 0.21)   | 0.64-0.76<br>(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<br>(mean = 0.09) | <0.21-<0.24<br>(mean = 0.22) | <0.65-<0.77<br>(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                                                                                        |                                                                                                                                                           |
|------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>RESIDUE DEFINITION FOR ENFORCEMENT</b><br>Primary crops and rotational crops                      | Fluopyram                                                                                                                                                 |
| <b>RESIDUE DEFINITION FOR RISK ASSESSMENT</b><br>Crop Groups 6 (Legume Vegetables) and 20 (Oilseeds) | Fluopyram including the metabolite fluopyram-benzamide (expressed as parent equivalent)                                                                   |
| All other crops                                                                                      | Fluopyram                                                                                                                                                 |
| <b>METABOLIC PROFILE IN DIVERSE CROPS</b>                                                            | Similar in grapes, potatoes, beans, red bell peppers                                                                                                      |
| ANIMAL STUDIES                                                                                       |                                                                                                                                                           |
| <b>RESIDUE DEFINITION FOR ENFORCEMENT</b><br>Ruminants and poultry                                   | Fluopyram including the metabolite fluopyram-benzamide (expressed as parent equivalent)                                                                   |
| <b>RESIDUE DEFINITION FOR RISK ASSESSMENT</b><br>Poultry tissues and eggs                            | Fluopyram including the metabolites fluopyram-benzamide and fluopyram-olefines (total of 2 isomers) (expressed as parent equivalent)                      |
| Ruminant tissues and milk                                                                            | Fluopyram including the metabolites fluopyram-benzamide, fluopyram-olefines (total of 2 isomers) and fluopyram-7-hydroxy (expressed as parent equivalent) |

|                                                                                                                                                                         |                      |                                                       |                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------|-------------------------------------------------------|-----------------------|
| <b>METABOLIC PROFILE IN ANIMALS</b>                                                                                                                                     |                      | Similar in goat, hen, rat                             |                       |
| <b>FAT SOLUBLE RESIDUE</b>                                                                                                                                              |                      | No                                                    |                       |
| <b>DIETARY RISK FROM FOOD AND WATER</b>                                                                                                                                 |                      |                                                       |                       |
| <b>Refined chronic dietary risk</b><br><br>ADI = 0.012 mg/kg bw/day<br><br>Estimated chronic drinking water concentration = 104 µg a.i./L                               | <b>POPULATION</b>    | <b>ESTIMATED RISK</b>                                 |                       |
|                                                                                                                                                                         |                      | <b>% of ACCEPTABLE DAILY INTAKE (ADI)</b>             |                       |
|                                                                                                                                                                         |                      | <b>Food Only</b>                                      | <b>Food and Water</b> |
|                                                                                                                                                                         | 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                                                  |                       |
| <b>Total population</b>                                                                                                                                                 | 1.3                  | 19.6                                                  |                       |
| <b>Basic acute dietary exposure analysis, 95<sup>th</sup> percentile</b><br><br>Estimated acute drinking water concentration = 106 µg a.i./L<br><br>ARfD = 0.5 mg/kg bw | <b>POPULATION</b>    | <b>ESTIMATED RISK</b>                                 |                       |
|                                                                                                                                                                         |                      | <b>% of ACUTE REFERENCE DOSE (ARfD)</b>               |                       |
|                                                                                                                                                                         |                      | <b>Food Only</b>                                      | <b>Food and Water</b> |
|                                                                                                                                                                         | 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                                                   |                       |
| <b>Total population</b>                                                                                                                                                 | 4.4                  | 5.0                                                   |                       |
| <b>Refined chronic cancer dietary risk</b><br><br>$Q_1^* = 0.0172 \text{ (mg/kg bw/day)}^{-1}$<br><br>Estimated chronic drinking water concentration = 2.93 µg a.i./L   | <b>POPULATION</b>    | <b>ESTIMATED RISK</b>                                 |                       |
|                                                                                                                                                                         |                      | <b>Adjusted for Limited 3-Year Application Period</b> |                       |
|                                                                                                                                                                         |                      | <b>Food and Water</b>                                 |                       |
| <b>Total population</b>                                                                                                                                                 | $1 \times 10^{-6}$   |                                                       |                       |

**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<br>pH 7 → 16 mg/L<br>pH 9 → 15 mg/L                                                 | soluble under environmentally relevant pH conditions                |
| Vapour pressure/volatility | 20°C → $1.2 \times 10^{-6}$ Pa<br>25°C → $3.1 \times 10^{-6}$ Pa<br>50°C → $2.9 \times 10^{-4}$ Pa | non-volatile under field conditions                                 |
| Henry's Law Constant       | 20°C → $2.98 \times 10^{-5}$ Pa m <sup>3</sup> mol <sup>-1</sup>                                   | low potential for volatilization from moist soil and water surfaces |

| Parameter                                 | Values                   | Interpretation                                                   |
|-------------------------------------------|--------------------------|------------------------------------------------------------------|
| UV absorption                             | < 292 nm                 | low potential for phototransformation                            |
| pK <sub>a</sub> (at 23°C)                 | 0.5                      | does not dissociate under environmentally relevant pH conditions |
| K <sub>ow</sub> /log K <sub>ow</sub>      | 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 <sub>50</sub> (days)                                                                                                                        | DT <sub>90</sub> (days)                              | Kinetic Model |       |     |
|-----------------------|--------------------------------------------|--------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------|---------------|-------|-----|
| <b>Soils</b>          |                                            |                                                                    |                                                                                                                                                |                                                      |               |       |     |
| 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 1 <sup>st</sup> year: 29% of 0-day 1 <sup>st</sup> application<br>end of 2 <sup>nd</sup> year: 57% of 0-day 2 <sup>nd</sup> application |                                                      |               |       |     |
|                       |                                            | Tarascon, France [silt loam]                                       | end of 1 <sup>st</sup> year: 53% of 0-day 1 <sup>st</sup> application<br>end of 2 <sup>nd</sup> year: 59% of 0-day 2 <sup>nd</sup> application |                                                      |               |       |     |
| Field studies: US     | dissipation/accumulation: AE C656948 500SC | Washington [sandy loam]                                            | 163                                                                                                                                            | DT <sub>75</sub> : 816<br>DT <sub>90</sub> : >1000   | DFOP          |       |     |
|                       |                                            | New York [loamy sand]                                              | 539                                                                                                                                            | DT <sub>75</sub> : >1000<br>DT <sub>90</sub> : >1000 | DFOP          |       |     |
|                       |                                            | North Dakota [loam]                                                | 83                                                                                                                                             | DT <sub>75</sub> : >1000<br>DT <sub>90</sub> : >1000 | DFOP          |       |     |
|                       |                                            | Georgia [loamy sand]                                               | 24                                                                                                                                             | DT <sub>75</sub> : 521<br>DT <sub>90</sub> : >1000   | DFOP          |       |     |
|                       |                                            | California [sandy loam]                                            | 174                                                                                                                                            | DT <sub>75</sub> : 688<br>DT <sub>90</sub> : >1000   | DFOP          |       |     |

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

**Table 22 Fate and Behaviour in the Aquatic Environment**

| Study                  | Label              | System                                                             | DT <sub>50</sub> (days)                                       | DT <sub>90</sub><br>(days) | Kinetic<br>model |
|------------------------|--------------------|--------------------------------------------------------------------|---------------------------------------------------------------|----------------------------|------------------|
| <b>Aquatic systems</b> |                    |                                                                    |                                                               |                            |                  |
| Hydrolysis             |                    | stable to hydrolysis under acidic, neutral and alkaline conditions |                                                               |                            |                  |
| Water photolysis       | phenyl and pyridyl | buffer solution (pH 7)                                             | 21 and 25<br>52 and 63 <sup>a</sup><br>81 and 97 <sup>b</sup> |                            | SFO              |
|                        | phenyl and pyridyl | natural water/sediment                                             | 21, 87 <sup>s</sup> and 135 <sup>b</sup>                      |                            | 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              |

<sup>a</sup>equivalent days of sunlight in Phoenix, Arizona

<sup>b</sup>Equivalent days of sunlight in Athens, Greece

**Table 23 Maximum Concentrations of Transformation Products in Soil and Water**

| Property                    | Transformation products                    |                                                                 |
|-----------------------------|--------------------------------------------|-----------------------------------------------------------------|
|                             | Major                                      | Minor                                                           |
| <b>Soil</b>                 |                                            |                                                                 |
| 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**<br>AE C656948- pyridyl-carboxylic acid** |
| <b>Water</b>                |                                            |                                                                 |
| 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

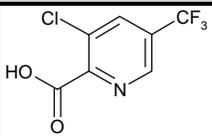
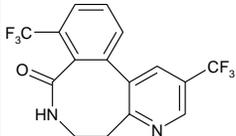
(): % of 0-day concentration

\*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 <sub>16</sub> H <sub>11</sub> ClF <sub>6</sub> N <sub>2</sub> O<br>396.72 g/mol              |
| Fluopyram - 7-hydroxy | N-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]-2-hydroxyethyl}-2-(trifluoromethyl)benzamide |           | C <sub>16</sub> H <sub>11</sub> ClF <sub>6</sub> N <sub>2</sub> O <sub>2</sub><br>412.72 g/mol |
| Fluopyram-benzamide   | 2-trifluoromethyl benzamide                                                                  |           | C <sub>8</sub> H <sub>6</sub> F <sub>3</sub> NO<br>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 <sub>7</sub> H <sub>3</sub> Cl F <sub>3</sub> N O <sub>2</sub><br>225.26 g/mol |
| Fluopyram-lactame                   | 2,9-bis(trifluoromethyl)-6,7-dihydropyrido[2,3-e][2]benzazocin-8(5H)-one |  | C <sub>16</sub> H <sub>10</sub> F <sub>6</sub> N <sub>2</sub> O<br>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<sup>3</sup>

\*\*\* 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 |
| <b>2 × 0.25 kg a.i./ha, at 7-day intervals</b> |                 |         |        |        |        |        |
| Potato-PEI                                     | 299             | 290     | 261    | 253    | 252    | 244    |

<sup>1</sup>Vulnerable scenario used in this Level 1 aquatic eco-scenario modelling.

**Table 27 EECs in Vegetation and Insects after a Direct Over-Spray<sup>1</sup> (Luna Privilege)**

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

<sup>1</sup> 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)

<sup>a</sup> based on correlations reported by Hoerger and Kenaga (1972) and Kenaga (1973)

<sup>b</sup> fresh to dry weight ratios from Harris (1975)

<sup>c</sup> 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 #             |
|---------------------------------------------------------------|---------------------------------------|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|--------------------|
| <b>Invertebrates</b>                                          |                                       |                  |                                                                                                                                                                                                     |                       |                    |
| Earthworm<br>( <i>Eisenia fetida andrei</i> )                 | 14-d acute                            | AE C656948       | LC <sub>50</sub> : >1000 mg a.i./kg dw soil<br>NOAEC: 100 mg a.i./kg dw soil<br>EC <sub>50</sub> : >1000 mg a.i./kg dw soil                                                                         | N/A                   | 1599606            |
|                                                               | 14-d acute                            | Luna Privilege G | LC <sub>50</sub> : >415 mg a.i./kg dw soil<br>EC <sub>50</sub> : >415 mg a.i./kg dw soil<br>NOAEC: 73.87a.i./kg dw soil                                                                             | N/A                   | 1599293            |
|                                                               | reproduction<br>(number of juveniles) | Luna Privilege G | EC <sub>50</sub> : >20.3 mg a.i./kg dw soil;<br>NOAEC: 11.4 mg a.i./kg dw soil                                                                                                                      | N/A                   | 1599294<br>1599589 |
| Honeybees<br>( <i>Apis mellifera</i> L.)                      | 48-h acute oral                       | AE C656948       | LC <sub>50</sub> : >102.3 µg a.i./bee<br>NOAEL: 102.3 µg a.i./bee<br>LOAEL: >102.3 µg a.i./bee                                                                                                      | relatively nontoxic   | 1599733            |
|                                                               | 48-h acute contact                    | AE C656948       | LD <sub>50</sub> : >100 µg a.i./bee<br>NOAEL: 100 µg a.i./bee<br>LOAEL: >100 µg a.i./bee                                                                                                            | relatively nontoxic   |                    |
|                                                               | 48-h acute contact and Oral           | Luna Privilege G | Contact: LD <sub>50</sub> : >83.2 µg a.i./bee<br>NOAEL: 83.2 µg a.i./bee<br>LOAEL: >83.2 µg a.i./bee<br>Oral: LC <sub>50</sub> : >89 µg a.i./bee<br>NOAEL: 89 µg a.i./bee<br>LOAEL: >89 µg a.i./bee | relatively nontoxic   | 1599290            |
| Parasitic wasp<br>( <i>Aphidius rhopalosiphi</i> )            | acute                                 | Luna Privilege G | LR <sub>50</sub> : >1008 g a.i./ha                                                                                                                                                                  | N/A                   | 1599729            |
|                                                               | chronic (reproduction)                |                  | ER <sub>50</sub> : >1008 g a.i./ha                                                                                                                                                                  | N/A                   | 1599291            |
| Predatory mite<br>( <i>Typhlodromus pyri</i> )                | acute                                 | Luna Privilege G | LR <sub>50</sub> : >1008 g a.i./ha                                                                                                                                                                  | N/A                   | 1599727            |
|                                                               | Chronic (reproduction)                |                  | NOAEL: 1008 g a.i./ha                                                                                                                                                                               | N/A                   | 1599292            |
| <b>Other soil invertebrates</b>                               |                                       |                  |                                                                                                                                                                                                     |                       |                    |
| Rove beetle<br>( <i>Aleochara bilineata</i> )                 | chronic (reproduction)                | Luna Privilege G | ER <sub>50</sub> : >1008 g a.i./ha                                                                                                                                                                  | N/A                   | 1599634<br>1599295 |
| Soil mite<br><i>Hypoaspis aculeifer</i> (Acari laelapidae)    | 14-d reproduction test                | Luna Privilege G | LC <sub>50</sub> > 415 mg a.i./kg dw soil<br>NOEC: 415 mg a.i./kg dw soil                                                                                                                           | N/A                   | 1599296            |
| Springtail<br><i>Folsomia candida</i> (Collembola isotomidae) | chronic (reproduction)                | Luna Privilege G | NOEC: 103.7 mg a.i./kg dw soil                                                                                                                                                                      | N/A                   | 1599297            |
| <b>Birds</b>                                                  |                                       |                  |                                                                                                                                                                                                     |                       |                    |
| Bobwhite quail<br>( <i>Colinus virginianus</i> )              | acute                                 | AE C656948       | LD <sub>50</sub> : >2000 mg a.i./kg bw<br>NOAEL: <500 mg a.i./kg bw                                                                                                                                 | practically non-toxic | 1599536            |
|                                                               | dietary                               | AE C656948       | LC <sub>50</sub> : >4785 mg a.i./kg diet<br>LD <sub>50</sub> : 1845.4 mg a.i./kg bw/day<br>LOAEC: 279 mg a.i./kg diet<br>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)<br>NOAEL: 4.12 mg a.i./kg bw/day<br>LOAEC: 75.7 mg a.i./kg diet<br>LOAEL: 6.8 mg a.i./kg bw/day                     | N/A                   | 1599605            |
| Mallard duck<br>( <i>Anas platyrhynchos</i> ) | dietary            | AE C656948                  | LC <sub>50</sub> : >4604.5 mg a.i./kg diet<br>LD <sub>50</sub> : 1642.7 mg a.i./kg bw/day<br>NOAEC: 2307.1 mg a.i./kg diet<br>LOAEC: 4604.5 mg a.i./kg diet            | practically non-toxic | 1599600            |
|                                               | reproduction       | AE C656948                  | NOAEC: 183 mg a.i./kg diet (survivor weights)<br>NOAEL: 18.46 mg a.i./kg bw/day<br>LOAEC: 428 mg a.i./kg diet                                                          | N/A                   | 1599731            |
| <b>Mammals</b>                                |                    |                             |                                                                                                                                                                        |                       |                    |
| Rat                                           | acute oral         | AE C 656948, Luna Privilege | LD <sub>50</sub> : >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                                                                                                                                            |                       |                    |
| <b>Vascular plants</b>                        |                    |                             |                                                                                                                                                                        |                       |                    |
| Vascular plant                                | seedling emergence | Luna Privilege G            | <b>Monocot</b> , most sensitive: none<br>EC <sub>25</sub> : > 500 g a.i./ha<br><b>Dicot</b> : most sensitive: Buckwheat (Biomass)<br>EC <sub>25</sub> : >500 g a.i./ha | N/A                   | 1599302<br>1599591 |
|                                               | vegetative vigour  | Luna Privilege G            | <b>Monocot</b> , most sensitive: none<br>EC <sub>25</sub> : > 250 g a.i./ha<br><b>Dicot</b> : most sensitive: none<br>EC <sub>25</sub> : >250g a.i./ha                 | N/A                   | 1599301<br>1599590 |

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

| Organism                               | Exposure               | Test Substance | Tox Value for RQ                                 | EEC                  | RQ    |
|----------------------------------------|------------------------|----------------|--------------------------------------------------|----------------------|-------|
| Earthworm<br>( <i>E. fetida</i> )      | acute                  | Luna Privilege | LC <sub>50</sub> ×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<br>( <i>A. mellifera</i> L.) | acute contact          | Luna Privilege | LD <sub>50</sub> : 93.2 kg a.i./ha**             | 0.4039 kg a.i./ha    | 0.004 |
| Predatory mite<br>( <i>T. pyri</i> )   | acute                  | Luna Privilege | LR <sub>50</sub> : >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<sub>50</sub> 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   |
|-----------------------------------|----------------------------|-----------------------------|---------------------|------|
| <b>Small Bird (0.02 kg)</b>       |                            |                             |                     |      |
| Acute                             | 200.00*                    | Insectivore (small insects) | 20.35               | 0.10 |
| Reproduction                      | 4.12                       | Insectivore (small insects) | 20.35               | 4.94 |
| <b>Medium Sized Bird (0.1 kg)</b> |                            |                             |                     |      |

| Effects                        | Toxicity<br>(mg a.i./kg bw/d) | Feeding Guild (food item)   | EDE<br>(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 |
| <b>Large Sized Bird (1 kg)</b> |                               |                             |                        |      |
| 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |      |                    |      |                    |      |                   |      | Mean Residues |      |                    |      |                    |      |                   |      |
|-----------------------------------|-------------------------------------|-----------------------------|------------------|------|--------------------|------|--------------------|------|-------------------|------|---------------|------|--------------------|------|--------------------|------|-------------------|------|
|                                   |                                     |                             | On-field         |      | Off-field<br>(74%) |      | Off-field<br>(59%) |      | Off-field<br>(6%) |      | On-field      |      | Off-field<br>(74%) |      | Off-field<br>(59%) |      | Off-field<br>(6%) |      |
|                                   |                                     |                             | EDE              | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   | EDE           | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   |
| <b>Small Bird (0.02 kg)</b>       |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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 |
| <b>Medium Sized Bird (0.1 kg)</b> |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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 |
| <b>Large Sized Bird (1 kg)</b>    |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |      |                    |      |                    |      |                   |      | Mean Residues |      |                    |      |                    |      |                   |      |
|-----------------------------------|-------------------------------------|-----------------------------|------------------|------|--------------------|------|--------------------|------|-------------------|------|---------------|------|--------------------|------|--------------------|------|-------------------|------|
|                                   |                                     |                             | On-field         |      | Off-field<br>(74%) |      | Off-field<br>(59%) |      | Off-field<br>(6%) |      | On-field      |      | Off-field<br>(74%) |      | Off-field<br>(59%) |      | Off-field<br>(6%) |      |
|                                   |                                     |                             | EDE              | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   | EDE           | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   |
| <b>Small Bird (0.02 kg)</b>       |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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 |
| <b>Medium Sized Bird (0.1 kg)</b> |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |

| Effects                        | Toxicity<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |      |                    |      |                    |      |                   |      | Mean Residues |      |                    |      |                    |      |                   |      |
|--------------------------------|-------------------------------------|-----------------------------|------------------|------|--------------------|------|--------------------|------|-------------------|------|---------------|------|--------------------|------|--------------------|------|-------------------|------|
|                                |                                     |                             | On-field         |      | Off-field<br>(74%) |      | Off-field<br>(59%) |      | Off-field<br>(6%) |      | On-field      |      | Off-field<br>(74%) |      | Off-field<br>(59%) |      | Off-field<br>(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 |
| <b>Large Sized Bird (1 kg)</b> |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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<br>(mg a.i./kg bw/d) | Feeding Guild (food item)   | EDE<br>(mg a.i./kg bw) | RQ   |
|---------------------------------------|-------------------------------|-----------------------------|------------------------|------|
| <b>Small Mammal (0.015 kg)</b>        |                               |                             |                        |      |
| Acute                                 | 200.00*                       | Insectivore (small insects) | 11.71                  | 0.06 |
| Reproduction                          | 13.90                         | Insectivore (small insects) | 11.71                  | 0.84 |
| <b>Medium Sized Mammal (0.035 kg)</b> |                               |                             |                        |      |
| Acute                                 | 200.00*                       | Herbivore (short grass)     | 36.67                  | 0.18 |
| Reproduction                          | 13.90                         | Herbivore (short grass)     | 36.67                  | 2.64 |
| <b>Large Sized Mammal (1 kg)</b>      |                               |                             |                        |      |
| 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |      |                    |      |                    |      |                   |      | Mean Residues |      |                    |      |                    |      |                   |      |
|---------------------------------------|-------------------------------------|-----------------------------|------------------|------|--------------------|------|--------------------|------|-------------------|------|---------------|------|--------------------|------|--------------------|------|-------------------|------|
|                                       |                                     |                             | On-field         |      | Off Field<br>(74%) |      | Off Field<br>(59%) |      | Off Field<br>(6%) |      | On-field      |      | Off Field<br>(74%) |      | Off Field<br>(59%) |      | Off Field<br>(6%) |      |
|                                       |                                     |                             | EDE              | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   | EDE           | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   |
| <b>Small Mammal (0.015 kg)</b>        |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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 |
| <b>Medium Sized Mammal (0.035 kg)</b> |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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 |
| <b>Large Sized Mammal (1 kg)</b>      |                                     |                             |                  |      |                    |      |                    |      |                   |      |               |      |                    |      |                    |      |                   |      |
| 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |      |                    |      |                    |      |                   |       | Mean Residues |      |                    |      |                    |       |                   |       |
|---------------------------------------|-------------------------------------|-----------------------------|------------------|------|--------------------|------|--------------------|------|-------------------|-------|---------------|------|--------------------|------|--------------------|-------|-------------------|-------|
|                                       |                                     |                             | On-field         |      | Off Field<br>(74%) |      | Off Field<br>(59%) |      | Off Field<br>(6%) |       | On-field      |      | Off Field<br>(74%) |      | Off Field<br>(59%) |       | Off Field<br>(6%) |       |
|                                       |                                     |                             | EDE              | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ    | EDE           | RQ   | EDE                | RQ   | EDE                | RQ    | EDE               | RQ    |
| <b>Small Mammal (0.015 kg)</b>        |                                     |                             |                  |      |                    |      |                    |      |                   |       |               |      |                    |      |                    |       |                   |       |
| 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 |
| <b>Medium Sized Mammal (0.035 kg)</b> |                                     |                             |                  |      |                    |      |                    |      |                   |       |               |      |                    |      |                    |       |                   |       |
| 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  |
| <b>Large Sized Mammal (1 kg)</b>      |                                     |                             |                  |      |                    |      |                    |      |                   |       |               |      |                    |      |                    |       |                   |       |
| 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |      |                    |      |                    |      |                   |       | Mean Residues |      |                    |      |                    |       |                   |       |
|---------|-------------------------------------|-----------------------------|------------------|------|--------------------|------|--------------------|------|-------------------|-------|---------------|------|--------------------|------|--------------------|-------|-------------------|-------|
|         |                                     |                             | On-field         |      | Off Field<br>(74%) |      | Off Field<br>(59%) |      | Off Field<br>(6%) |       | On-field      |      | Off Field<br>(74%) |      | Off Field<br>(59%) |       | Off Field<br>(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 <sub>25</sub> : 500 g a.i./ha | 497.76 g a.i./ha | <b>1.00</b> |
|                 | vegetative vigour  | Luna Privilege A G | EC <sub>25</sub> : 250 g a.i./ha | 403.9 g a.i./ha* | <b>1.62</b> |

\*with a default foliar half-life of 10 days

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

|                                                                                               | Airblast Early<br>(74% drift) | Airblast Late<br>(59% drift) | Ground Boom<br>(6% drift) |
|-----------------------------------------------------------------------------------------------|-------------------------------|------------------------------|---------------------------|
| Application rate<br>(250 g a.i./ha)                                                           | 185 g a.i./ha                 | 147.5 g a.i./ha              | 15.00 g a.i./ha           |
| <b>Seedling Emergence</b>                                                                     |                               |                              |                           |
| Cumulative application rate<br>(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 <sub>25</sub> of 500 g a.i./ha for seedling emergence                              | 0.77                          | 0.59                         | 0.06                      |
| Risk                                                                                          | no risk                       | no risk                      | no risk                   |
| <b>Vegitative vigour</b>                                                                      |                               |                              |                           |
| Cumulative application rate<br>(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 <sub>25</sub> of 250 g a.i./ha for vegetative vogueur                              | 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<sup>3</sup>

\*\*\* 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 <sup>a</sup><br>(mg a.i./kg fw) | Fresh/Dry<br>Weight Ratios | EEC Direct Overspray<br>(mg a.i./kg dw)<br>Maximum Residues | Mean EEC<br>(mg a.i./kg dw)<br>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                                      |

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

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

| Effects                           | Toxicity<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |             |                    |             |                    |             |                   |      | Mean Residues |             |                    |             |                    |      |                   |      |
|-----------------------------------|-------------------------------------|-----------------------------|------------------|-------------|--------------------|-------------|--------------------|-------------|-------------------|------|---------------|-------------|--------------------|-------------|--------------------|------|-------------------|------|
|                                   |                                     |                             | On-field         |             | Off-field<br>(74%) |             | Off-field<br>(59%) |             | Off-field<br>(6%) |      | On-field      |             | Off Field<br>(74%) |             | Off Field<br>(59%) |      | Off Field<br>(6%) |      |
|                                   |                                     |                             | EDE              | RQ          | EDE                | RQ          | EDE                | RQ          | EDE               | RQ   | EDE           | RQ          | EDE                | RQ          | EDE                | RQ   | EDE               | RQ   |
| <b>Small Bird (0.02 kg)</b>       |                                     |                             |                  |             |                    |             |                    |             |                   |      |               |             |                    |             |                    |      |                   |      |
| Reproduction                      | 4.12                                | Insectivore (small insects) | 11.95            | <b>2.90</b> | 8.84               | <b>2.15</b> | 7.05               | <b>1.71</b> | 0.72              | 0.17 | 6.66          | <b>1.62</b> | 4.93               | <b>1.20</b> | 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             | <b>1.45</b> | 4.42               | <b>1.07</b> | 3.53               | 0.86        | 0.36              | 0.09 | 2.85          | 0.69        | 2.11               | 0.51        | 1.68               | 0.41 | 0.17              | 0.04 |
| <b>Medium Sized Bird (0.1 kg)</b> |                                     |                             |                  |             |                    |             |                    |             |                   |      |               |             |                    |             |                    |      |                   |      |
| Reproduction                      | 4.12                                | Insectivore (small insects) | 9.33             | <b>2.26</b> | 6.90               | 1.68        | 5.50               | <b>1.34</b> | 0.56              | 0.14 | 5.20          | <b>1.26</b> | 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |             |                    |             |                    |             |                   |      | Mean Residues |      |                    |      |                    |      |                   |      |
|--------------------------------|-------------------------------------|-----------------------------|------------------|-------------|--------------------|-------------|--------------------|-------------|-------------------|------|---------------|------|--------------------|------|--------------------|------|-------------------|------|
|                                |                                     |                             | On-field         |             | Off-field<br>(74%) |             | Off-field<br>(59%) |             | Off-field<br>(6%) |      | On-field      |      | Off Field<br>(74%) |      | Off Field<br>(59%) |      | Off Field<br>(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             | <b>1.13</b> | 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 |
| <b>Large Sized Bird (1 kg)</b> |                                     |                             |                  |             |                    |             |                    |             |                   |      |               |      |                    |      |                    |      |                   |      |
| 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             | <b>2.36</b> | 7.20               | <b>1.75</b> | 5.74               | <b>1.39</b> | 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             | <b>1.44</b> | 4.40               | <b>1.07</b> | 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             | <b>2.19</b> | 6.66               | <b>1.62</b> | 5.31               | <b>1.29</b> | 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<br>(mg<br>a.i./kg<br>bw/d) | Food Guild (food item)      | Maximum Residues |             |                    |             |                    |             |                   |      | Mean Residues |      |                    |      |                    |      |                   |      |
|-----------------------------------|-------------------------------------|-----------------------------|------------------|-------------|--------------------|-------------|--------------------|-------------|-------------------|------|---------------|------|--------------------|------|--------------------|------|-------------------|------|
|                                   |                                     |                             | On-field         |             | Off-field<br>(74%) |             | Off-field<br>(59%) |             | Off-field<br>(6%) |      | On-field      |      | Off Field<br>(74%) |      | Off Field<br>(59%) |      | Off Field<br>(6%) |      |
|                                   |                                     |                             | EDE              | RQ          | EDE                | RQ          | EDE                | RQ          | EDE               | RQ   | EDE           | RQ   | EDE                | RQ   | EDE                | RQ   | EDE               | RQ   |
| <b>Small Bird (0.02 kg)</b>       |                                     |                             |                  |             |                    |             |                    |             |                   |      |               |      |                    |      |                    |      |                   |      |
| Reproduction                      | 6.8                                 | Insectivore (small insects) | 11.95            | <b>1.76</b> | 8.84               | <b>1.30</b> | 7.05               | <b>1.04</b> | 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 |
| <b>Medium Sized Bird (0.1 kg)</b> |                                     |                             |                  |             |                    |             |                    |             |                   |      |               |      |                    |      |                    |      |                   |      |
| Reproduction                      | 6.8                                 | Insectivore (small insects) | 9.33             | <b>1.37</b> | 6.90               | <b>1.01</b> | 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 |
| <b>Large Sized Bird (1 kg)</b>    |                                     |                             |                  |             |                    |             |                    |             |                   |      |               |      |                    |      |                    |      |                   |      |
| 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             | <b>1.43</b> | 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             | <b>1.32</b> | 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<br>(mg a.i./kg bw/d) | Feeding Guild (food item)   | EDE<br>(mg a.i./kg bw) | RQ          |
|---------------------------------------|-------------------------------|-----------------------------|------------------------|-------------|
| <b>Small Mammal (0.015 kg)</b>        |                               |                             |                        |             |
| Acute                                 | 200.00                        | Insectivore (small insects) | 6.87                   | 0.03        |
| Reproduction                          | 13.90                         | Insectivore (small insects) | 6.87                   | 0.49        |
| <b>Medium Sized Mammal (0.035 kg)</b> |                               |                             |                        |             |
| Acute                                 | 200.00                        | Herbivore (short grass)     | 21.53                  | 0.11        |
| Reproduction                          | 13.90                         | Herbivore (short grass)     | 21.53                  | <b>1.55</b> |
| <b>Large Sized Mammal (1 kg)</b>      |                               |                             |                        |             |
| 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<br>(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   |  |
| <b>Medium Mammal (0.055 kg)</b> |                               |                             |                  |             |                 |             |                 |      |                |      |          |               |                 |      |                 |      |                |      |  |
| 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            | <b>1.55</b> | 15.94           | <b>1.15</b> | 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            | <b>1.43</b> | 14.74           | <b>1.06</b> | 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<br>(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   |  |
| <b>Medium sized Mammal (0.035 kg)</b> |                               |                             |                  |      |                 |      |                 |      |                |      |          |               |                 |      |                 |      |                |      |  |
| 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<br>SC 500A G | EC <sub>25</sub> : 500 g a.i./ha | 491.12 g a.i./ ha* | 0.98 |
|                 | vegetative vigour  | AE C656948<br>SC 500A G | EC <sub>25</sub> : 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<br>(mg a.i./kg bw/d) | Feeding Guild (food item)   | EDE<br>(mg a.i./kg bw) | RQ          |
|-----------------------------------|-------------------------------|-----------------------------|------------------------|-------------|
| <b>Small Bird (0.02 kg)</b>       |                               |                             |                        |             |
| Acute                             | 200.00                        | Insectivore (small insects) | 12.21                  | 0.06        |
| Reproduction                      | 4.12                          | Insectivore (small insects) | 12.21                  | <b>2.96</b> |
| <b>Medium Sized Bird (0.1 kg)</b> |                               |                             |                        |             |
| Acute                             | 200.00                        | Insectivore (small insects) | 9.53                   | 0.05        |
| Reproduction                      | 4.12                          | Insectivore (small insects) | 9.53                   | <b>2.31</b> |
| <b>Large Sized Bird (1 kg)</b>    |                               |                             |                        |             |
| Acute                             | 200.00                        | Herbivore (short grass)     | 9.94                   | 0.05        |
| Reproduction                      | 4.12                          | Herbivore (short grass)     | 9.94                   | <b>2.41</b> |

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

| Effects                           | Toxicity<br>mg<br>a.i./kg<br>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   |
| <b>Small Bird (0.02 kg)</b>       |                                   |                             |                  |             |                |      |               |             |                |      |
| Reproduction                      | 4.12                              | Insectivore (small insects) | 12.21            | <b>2.96</b> | 0.73           | 0.18 | 6.81          | <b>1.65</b> | 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             | <b>1.48</b> | 0.37           | 0.09 | 2.91          | 0.71        | 0.17           | 0.04 |
| <b>Medium Sized Bird (0.1 kg)</b> |                                   |                             |                  |             |                |      |               |             |                |      |
| Reproduction                      | 4.12                              | Insectivore (small insects) | 9.53             | <b>2.31</b> | 0.57           | 0.14 | 5.31          | <b>1.29</b> | 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             | <b>1.16</b> | 0.29           | 0.07 | 2.27          | 0.55        | 0.14           | 0.03 |

| Effects                        | Toxicity<br>mg<br>a.i./kg<br>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   |
| <b>Large Sized Bird (1 kg)</b> |                                   |                             |                  |             |                |      |               |      |                |      |
| 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             | <b>2.41</b> | 0.60           | 0.14 | 3.53          | 0.86 | 0.21           | 0.05 |
|                                | 4.12                              | Herbivore (long grass)      | 6.07             | <b>1.47</b> | 0.36           | 0.09 | 1.98          | 0.48 | 0.12           | 0.03 |
|                                | 4.12                              | Herbivore (forage crops)    | 9.20             | <b>2.23</b> | 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   |
| <b>Small Bird (0.02 kg)</b>       |          |                             |                  |             |                |      |               |             |                |      |
| Reproduction                      | 6.8      | Insectivore (small insects) | 12.21            | <b>1.80</b> | 0.73           | 0.11 | 6.81          | <b>1.00</b> | 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 |
| <b>Medium Sized Bird (0.1 kg)</b> |          |                             |                  |             |                |      |               |             |                |      |
| Reproduction                      | 6.8      | Insectivore (small insects) | 9.53             | <b>1.40</b> | 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 |
| <b>Large Sized Bird (1 kg)</b>    |          |                             |                  |             |                |      |               |             |                |      |
| 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             | <b>1.46</b> | 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             | <b>1.35</b> | 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 | EC <sub>25</sub> : 500.00 g a.i./ha | 298.656 g a.i./ ha | <b>0.60</b> |
|                 | vegetative vigour  | AE C656948 SC 500A G | EC <sub>25</sub> :250.00g a.i./ha   | 242.345 g a.i./ha  | <b>0.97</b> |

**Table 51** Effects on Aquatic Organisms

| Organism                                                                  | Exposure                         | Test Substance                                | Endpoint Value                                                                                                                                        | Degree of Toxicity | PMRA #  |
|---------------------------------------------------------------------------|----------------------------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------|---------|
| <b>Freshwater species</b>                                                 |                                  |                                               |                                                                                                                                                       |                    |         |
| Rainbow trout<br>( <i>Oncorhynchus mykiss</i> )                           | acute (96 h)                     | AE C656948                                    | LC <sub>50</sub> : >1.78 mg a.i./L<br>NOAEC: 1.78 mg a.i./L                                                                                           | moderately toxic   | 1599539 |
|                                                                           | acute (96 h)                     | Luna Privilege G                              | LC <sub>50</sub> : >46.4 mg a.i./L<br>NOAEC: 1.31 mg a.i./L<br>EC <sub>50</sub> : 3.71 mg a.i./L (sub-lethal effects)                                 | slightly toxic     | 1599284 |
| Bluegill sunfish<br>( <i>Lepomis macrochirus</i> )                        | acute (96 h)                     | AE C656948                                    | LC <sub>50</sub> : >5.17 mg a.i./L<br>NOAEC: 5.17 mg a.i./L                                                                                           | moderately toxic   | 1599538 |
| Fathead minnow<br>( <i>Pimephales promelas</i> )                          | acute (96 h)                     | AE C656948                                    | LC <sub>50</sub> : >4.95 mg a.i./L<br>NOAEC: 4.95 mg a.i./L<br>EC <sub>50</sub> : >4.95 mg a.i./L                                                     | moderately toxic   | 1599543 |
| Fathead minnow<br>( <i>Pimephales promelas</i> )                          | chronic: early life stage (33 d) | AE C656948                                    | NOAEC: 0.135 mg a.i./L<br>LOAEC: 0.269 mg a.i./L                                                                                                      | N/A                | 1599730 |
| Daphnia<br>( <i>Daphnia magna</i> )                                       | acute (48 h)                     | AE C656948                                    | NOAEC: 17 mg a.i./L<br>EC <sub>50</sub> : >17 mg a.i./L                                                                                               | slightly toxic     | 1599541 |
|                                                                           | chronic<br>(Life cycle: 21 d)    | AE C656948                                    | NOAEC: 1.214 mg a.i./L<br>LOAEC: 2.996 mg a.i./L<br>21-d EC <sub>50</sub> : 2.700 mg a.i./L (reproduction)                                            | N/A                | 1599770 |
|                                                                           | acute (48 h)                     | Luna Privilege G                              | 48-h EC <sub>50</sub> : >38.2 mg a.i./L<br>NOAEC: 11.6 mg a.i./L                                                                                      | slightly toxic     | 1599285 |
| Freshwater green algae<br>( <i>Pseudokirchneriella subcapitata</i> )      | acute (96 h)                     | AE C656948                                    | NOAEC: 1.46 mg a.i./L<br>EC <sub>50</sub> : 4.3 mg a.i./L (Biomass)                                                                                   | N/A                | 1599864 |
|                                                                           | acute (72 h)                     | Luna Privilege G                              | NOAEC: 1.17 mg a.i./L<br>EC <sub>05</sub> : 1.0 mg a.i./L<br>EC <sub>50</sub> : 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<br>EC <sub>50</sub> : >8.87 mg a.i./L (growth inhibition)                                                                       | N/A                | 1599808 |
| Freshwater diatom<br>( <i>Navicula pelliculosa</i> )                      | acute (96 h)                     | AE C656948                                    | NOAEC: 2.47 mg a.i./L<br>EC <sub>50</sub> : 6.1 mg a.i./L (biomass)                                                                                   | N/A                | 1599862 |
| Freshwater blue-green algae<br>( <i>Anabaena flos-aquae</i> )             | acute (96 h)                     | AE C656948                                    | NOAEC: 9.69 mg a.i./L<br>EC <sub>50</sub> : >9.69 mg a.i./L<br>most sensitive end-point: none                                                         | N/A                | 1599863 |
| Duckweed ( <i>Lemna gibba</i> )                                           | acute (7 d)                      | AE C656948                                    | NOAEC: 0.278 mg a.i./L<br>EC <sub>05</sub> > 0.278 mg a.i./L<br>EC <sub>50</sub> : 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<br>EC <sub>05</sub> : 1.8 mg a.i./L<br>EC <sub>50</sub> : 2.9 mg a.i./L (frond number)                                          | N/A                | 1599303 |
| Sediment dwelling Freshwater chironomid<br>( <i>Chironomus riparius</i> ) | 28-d chronic                     | AE C656948                                    | <u>overlying water concentrations*</u><br>EC <sub>50</sub> (emergence ratio): >5.52 mg a.i./L<br>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 ( <i>Chironomus tentans</i> ) | 54-day life-cycle | AE C656948     | NOAEC (survival and emergences):<br>sediment: 26 mg a.i./kg<br>pore water: 3.8 mg a.i./L (TWA)<br>overlying water: 0.14 mg a.i./L                                                                                                                                                                                                                                                                            | N/A                | 1599614 |
| <b>Marine species</b>                                   |                   |                |                                                                                                                                                                                                                                                                                                                                                                                                              |                    |         |
| Sheepshead Minnow ( <i>Cyprinodon variegatus</i> )      | acute (96 h)      | AE C656948     | LC <sub>50</sub> : >0.98 mg a.i./L<br>NOAEC: 0.98 mg a.i./L<br>EC <sub>50</sub> : >0.98 mg a.i./L                                                                                                                                                                                                                                                                                                            | highly toxic       | 1599544 |
| Eastern Oyster ( <i>Crassostrea virginica</i> )         | acute (96 h)      | AE C656948     | EC <sub>50</sub> : >0.43 mg a.i./L NOAEC:<br>0.43 mg a.i./L<br>(shell deposition)                                                                                                                                                                                                                                                                                                                            | highly toxic       | 1599604 |
| Saltwater Mysid ( <i>Americamysis bahia</i> )           | acute (96 h)      | AE C656948     | LC <sub>50</sub> : >0.51 mg a.i./L<br>NOAEC: 0.27 mg a.i./L                                                                                                                                                                                                                                                                                                                                                  | highly toxic       | 1599603 |
| Saltwater Diatom ( <i>Skeletonema costatum</i> )        | acute (96 h)      | AE C656948     | EC <sub>50</sub> : > 1.13 mg a.i./L<br>NOAEC: 1.13 mg a.i./L (cell density, biomass, growth rate)<br>most sensitive end-point: none                                                                                                                                                                                                                                                                          | moderately toxic   | 1599865 |
| Marine amphipods ( <i>Leptocheirus plumulosus</i> )     | 10-d acute        | AE C656948     | <u>sediment concentrations</u><br>LC <sub>50</sub> mortality: >100 mg a.i./kg<br>NOAEC (mortality): 100 mg a.i./kg<br><br><u>Pore water concentrations</u><br>LC <sub>50</sub> mortality: >7.5 mg a.i./L<br>NOAEC (mortality): 7.5 mg a.i./L<br><br><u>Overlying water concentrations</u><br>LC <sub>50</sub> mortality: >1.6 mg a.i./L<br>NOAEC (mortality): 1.6 mg a.i./L                                  | moderately toxic   | 1599616 |
| Marine amphipods ( <i>Leptocheirus plumulosus</i> )     | 28-d chronic      | AE C656948     | <u>sediment concentrations</u><br>(Total radioactive residues equivalent to a.i.)<br>EC <sub>50</sub> growth: >92 mg a.i./kg<br>NOAEC (growth): 36 mg a.i./kg<br><br><u>pore water concentrations</u><br>EC <sub>50</sub> growth: >5.9 mg a.i./L<br>NOAEC (growth): 2.5 mg a.i./L<br><br><u>overlying water concentrations</u><br>EC <sub>50</sub> growth: >1.19 mg a.i./L<br>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<br>( <i>O. mykiss</i> )                               | acute                     | AE C656948       | (LC <sub>50</sub> /10): >0.178**                    | 0.062*                            | <0.35  |
| Bluegill sunfish<br>( <i>L. macrochirus</i> )                       | bioaccumulation study     | AE C656948       | BCF: 18                                             | low potential for bioaccumulation |        |
| Fathead minnow<br>( <i>P. promelas</i> )                            | chronic: early life stage | AE C656948       | NOAEC: 0.135                                        | 0.062*                            | 0.46   |
| Sediment dwelling<br>( <i>C. riparius</i> )<br>( <i>C. tetans</i> ) | 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 <sub>50</sub> /10): >0.178**                    | 0.33 <sup>£</sup>                 | <1.85  |
|                                                                     | chronic                   | AE C656948       | NOAEC: 0.135                                        | 0.33 <sup>£</sup>                 | 2.44   |
| Daphnia<br>( <i>D. magna</i> )                                      | Acute                     | AE C656948       | (EC <sub>50</sub> /2): >8.5***                      | 0.062*                            | <0.017 |
|                                                                     | chronic                   | AE C656948       | NOAEC: 1.214                                        | 0.062*                            | 0.05   |
| Freshwater green algae ( <i>P. subcapitata</i> )                    | acute                     | Luna Privilege G | (EC <sub>50</sub> /2): 1.7***                       | 0.062*                            | 0.04   |
| Freshwater diatom<br>( <i>N. pelliculosa</i> )                      | acute                     | AE C656948       | (EC <sub>50</sub> /2): 3.1***                       | 0.062                             | 0.02   |
| Duckweed ( <i>L. gibba</i> )                                        | acute                     | AE C656948       | (EC <sub>50</sub> /2): 1.3***                       | 0.062*                            | 0.05   |
| Sheepshead Minnow<br>( <i>C. variegatus</i> )                       | acute                     | AE C656948       | (LC <sub>50</sub> /10): >0.098**                    | 0.062*                            | <0.63  |
| Eastern Oyster<br>( <i>C. virginica</i> )                           | acute                     | AE C656948       | (LC <sub>50</sub> /2): 0.22***                      | 0.062*                            | 0.28   |
| Saltwater Diatom<br>( <i>S. costatum</i> )                          | acute                     | AE C656948       | (EC <sub>50</sub> /2): >0.57***                     | 0.062*                            | <0.11  |
| Marine amphipods<br>( <i>Leptocheirus plumulosus</i> )              | acute                     | AE C656948       | (LC <sub>50</sub> /2): >0.8***<br>(overlying water) | 0.062*                            | <0.08  |
|                                                                     | chronic                   | AE C656948       | NOAEC: 0.55<br>(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 <sub>50</sub> /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<br>(74% drift) | Airblast late<br>(59% drift) | Ground boom<br>(6% drift) |
|---------------------------------------------------------------|-------------------------------|------------------------------|---------------------------|
| Application rate<br>(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<br>(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 <sub>50</sub> : 0.178 mg a.i./L)                  | <b>1.40</b>                   | <b>1.12</b>                  | 0.11                      |
| Chronic RQ (NOEC: 0.135 mg a.i./L)                            | <b>1.85</b>                   | <b>1.48</b>                  | 0.15                      |
| Risk                                                          | yes                           | yes                          | no                        |

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

|                                              | Screening level<br>(direct overspray) | Aerial application-in off-field<br>(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 <sub>50</sub> : 0.178 mg a.i./L) | <b>1.49</b>                           | 0.34                                           |
| Chronic RQ (NOEC: 0.135 mg a.i./L)           | <b>1.97</b>                           | 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 <sub>50</sub> /10): 0.178 | 0.2*            | <b>1.12</b> |
| Chronic  | AE C656948     | NOAEC: 0.135                  | 0.2*            | <b>1.48</b> |

\* 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 <sub>50</sub> /10): >0.178 | <b>0.179*</b>   | <b>&lt;1.00</b> |
| Chronic  | AE C656948     | NOAEC: 0.135                   | 0.157**         | <b>1.16</b>     |

\*\* 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 <sub>50</sub> :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<br>(Resistance Management Group) |
|------------|---------------------------------|-----------------------------------------------------|
| Watermelon | Powdery mildew <sup>1</sup>     | <i>Bacillus subtilis</i> QST 713 (44)               |
|            |                                 | chlorothalonil (M5)                                 |
|            |                                 | difenoconazole (3)                                  |
|            |                                 | folpet (M4)                                         |
|            |                                 | potassium bicarbonate (NC)                          |
|            |                                 | pyraclostrobin (22)                                 |
|            |                                 | <i>Streptomyces lydicus</i> WYEC 108 (NC)           |
|            | Botrytis grey mold <sup>1</sup> | ferbam (M3)                                         |
|            |                                 | <i>Gliocladium catenulatum</i> J1446 (NC)           |
|            |                                 | iprodione (2)                                       |

| Crops                                       | Diseases                                      | Active Ingredients<br>(Resistance Management Group) |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------------|
| Wine Grape                                  | Botrytis bunch rot / Grey mold <sup>1,3</sup> | <i>Bacillus subtilis</i> QST 713 (44)               |
|                                             |                                               | boscalid (7) + pyraclostrobin (11)                  |
|                                             |                                               | fenhexamid (17)                                     |
|                                             | Powdery mildew <sup>3</sup>                   | <i>Bacillus subtilis</i> 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)                  |
|                                             |                                               | quinoxifen (13)                                     |
| sulphur (M2)                                |                                               |                                                     |
| trifloxystrobin (11)                        |                                               |                                                     |
| Dry Bean<br>(Including Chickpea and Lentil) | White mold <sup>1,2</sup>                     | <i>Bacillus subtilis</i> QST 713 (44)               |
|                                             |                                               | boscalid (7)                                        |
|                                             |                                               | <i>Coniothyrium minitans</i> CON/M/91-08 (NC)       |
|                                             |                                               | cyprodinil (9) + fludioxonil (12)                   |
|                                             |                                               | dicloran (14)                                       |
|                                             |                                               | fluazinam (29)                                      |
|                                             |                                               | iprodione (2)                                       |
|                                             | vinclozolin (2)                               |                                                     |
|                                             | Ascochyta blight <sup>1,2</sup>               | azoxystrobin (11)                                   |
|                                             |                                               | pyraclostrobin (11)                                 |
|                                             | Mycosphaerella blight <sup>1,2</sup>          | azoxystrobin (11)                                   |
|                                             |                                               | pyraclostrobin (11)                                 |
|                                             | Powdery mildew <sup>1</sup>                   | azoxystrobin (11) + propiconazole (3)               |
| propiconazole (3)                           |                                               |                                                     |
| pyraclostrobin (11)                         |                                               |                                                     |
| Peanut                                      | Early Leaf Spot <sup>1</sup>                  | <i>Bacillus subtilis</i> QST 713 (44)               |
|                                             |                                               | prothioconazole (3)                                 |
|                                             | Late Leaf Spot <sup>1</sup>                   | <i>Bacillus subtilis</i> QST 713 (44)               |
| Apple                                       | Leaf scab <sup>1,3</sup>                      | <i>Bacillus subtilis</i> QST 713 (44)               |
|                                             |                                               | boscalid (7) + pyraclostrobin (11)                  |
|                                             |                                               | calcium polysulphide (M2)                           |
|                                             |                                               | captan (M4)                                         |
|                                             |                                               | cyprodinil (9)                                      |
|                                             |                                               | difenoconazole (3)                                  |
|                                             |                                               | dodine (M7)                                         |
|                                             |                                               | ferbam (M3)                                         |
| fluazinam (29)                              |                                               |                                                     |

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

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

<sup>1</sup>claim appears on the Luna Privilege label

<sup>2</sup>claim appears on the Propulse Fungicide label

<sup>3</sup>claim appears on the Luna Tranquility Fungicide label

<sup>4</sup> 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 <i>Canadian Environmental Protection Act</i> <sup>1</sup> | yes                                      |                                                             |                                       |
| Predominantly anthropogenic <sup>2</sup>                                                              | yes                                      |                                                             |                                       |
| Persistence <sup>3</sup> :                                                                            | soil                                     | half-life: $\geq 182$ days                                  | field DT <sub>50</sub> : 539 days     |
|                                                                                                       | water                                    | half-life: $\geq 182$ days                                  | half-life: 1470 days (water+sediment) |
|                                                                                                       | sediment                                 | half-life: $\geq 365$ days                                  | not available                         |
|                                                                                                       | air                                      | half-life $\geq 2$ days or evidence of long range transport | 1.7 to 2.6 days                       |
| Bioaccumulation <sup>4</sup>                                                                          | log K <sub>OW</sub> $\geq 5$             |                                                             | 3.3                                   |
|                                                                                                       | BCF $\geq 5000$                          |                                                             | 18                                    |
|                                                                                                       | BAF $\geq 5000$                          |                                                             |                                       |
| Is the chemical a TSMP Track 1 substance (all four criteria must be met)?                             | no, does not meet TSMP Track 1 criteria. |                                                             |                                       |

<sup>1</sup> 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).

<sup>2</sup> 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.

- <sup>3</sup> 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.
- <sup>4</sup> Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example,  $\log K_{ow}$ ).



## 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 – Tuberos 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);<br>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                                                                                                                                                                                                                                                  |
|----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1599498              | 2008, 1st amendment to report no. 20050612.01 - AE C656948; Substance, pure - AE C656948 00 1B99 0001- Vapour pressure A.4. (OECD 104), DACO: 2.14.9,IIA 2.3.1                                                                                             |
| 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                                                                                                   |
| 1599676              | 2008, Determination of [CBI removed] in active ingredient of agrochemicals [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI                                                                                                                                       |
| 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
- 1599749 2008, Fluopyram (AEC 656948) - Technical grade active substance - Manufacturing process, DACO: 2.11.1,2.11.2,2.11.3,2.11.4,IIA 1.8.1,IIA 1.8.2 CBI
- 1599755 2008, Fluopyram, AE C656948 - Auto-flammability (Bowes-Cameron-Cage test), DACO: 2.16,IIA 2.11.2
- 1599756 2008, Fluopyram, AE C656948 - Auto-flammability (solids - determination of relative self-ignition temperature) A.16., DACO: 2.16,IIA 2.11.2
- 1599757 2008, Fluopyram, AE C656948 - Flammability (solids) A.10., DACO: 2.16,IIA 2.11.1
- 1599758 2008, Fluopyram, AE C656948 - Oxidizing properties A.17., DACO: 2.16,IIA 2.15
- 1599764 2008, Henry's law constant of fluopyram (AE C656948) at pH 4, pH 7 and pH 9, DACO: 2.16,IIA 2.3.2
- 1599765 2008, Henry's law constant of fluopyram (AE C656948), DACO: 2.16,IIA 2.3.2
- 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
- 1599778 2008, Material accountability of fluopyram manufactured at Dormagen / Germany, DACO: 2.13.3,IIA 1.11.1 CBI
- 1599797 2008, Particle size, fiber length and diameter distribution of fluopyram technical, DACO: 2.16,IIA 2.18
- 1599798 2008, Partition coefficients 1-octanol / water of AE C656948 - (shake flask method), DACO: 2.14.11,IIA 2.8.1
- 1599807 2008, Physical characteristics color, physical state and odor of fluopyram (AE C656948) Technical substance and pure substance, DACO: 2.14.1,2.14.2,2.14.3,IIA 2.4.1,IIA 2.4.2
- 1599810 2008, Relative density of fluopyram (AE C656948), pure substance and technical substance, DACO: 2.14.6,IIA 2.2
- 1599814 2008, Solubility in organic solvents AE C656948 pure substance, DACO: 2.14.8,IIA 2.7
- 1599816 2007, Spectral data set of AE C656948, DACO: 2.13.2,2.14.12,IIA 2.5.1.1,IIA 2.5.1.2,IIA 2.5.1.3,IIA 2.5.1.4,IIA 2.5.1.5
- 1599817 2008, Stability to normal and elevated temperature, metals, and metal ions of Fluopyram, DACO: 2.14.13,IIA 2.17.2
- 1599820 2008, Storage stability of AE C656948 - Amendment no.1, DACO: 2.14.14,IIA 2.17.1

- 1599822 2008, Surface tension of fluopyram (AE C656948) technical substance, DACO: 2.16,IIA 2.14
- 1599833 2008, The oxidation or reduction properties of fluopyram (AE C656948), technical substance, DACO: 2.16,IIA 2.18
- 1599869 2008, UV/VIS spectral data set of fluopyram, DACO: 2.13.2,2.14.12,IIA 2.5.1.1,IIA 2.5.1.5
- 1599872 2008, Validation of [CBI removed] - Fluopyram - Byproducts in technical grade active substance [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI
- 1599873 2008, Validation of HPLC-method AM002705MP1 AE C656948 assay of technical grade active substance, DACO: 2.13.1,IIA 4.2.1
- 1599874 2008, Validation of [CBI removed] - Fluopyram - Byproducts in technical grade active substance [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI
- 1599875 2008, Validation of [CBI removed] - determination of [CBI removed] in technical grade active [CBI removed] in AE C656948 [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI
- 1599876 2008, Water solubility of AE C656948 at pH 4, pH 7, pH 9 and in distilled water (Flask method), DACO: 2.14.7,IIA 2.6
- 1745793 Draft Assessment Report of Fluopyram, DACO: 2.0,3.0 CBI
- 1762436 2009, Position Paper - Addressing the Identity of the Impurity [CBI removed], DACO: 2.13.2 CBI
- 1908576 2010, Composition Statement - Technical grade active substance - Fluopyram TC, AE C656948, DACO: 2.12.2,2.13.4,IIA 1.10.1,IIA 1.10.2 CBI
- 1908577 2010, Fluopyram (AEC 656948) Technical grade active substance - Discussion of the formation of impurities, DACO: 2.12.2,2.13.4,IIA 1.10.2 CBI
- 1908579 2010, 2nd Amendment to material accountability of fluopyram manufactured at Dormagen / Germany - Five batches of technical fluopyram, DACO: 2.13.3,IIA 1.11.1 CBI
- 1908580 2010, Material accountability of Fluopyram - re-analysis of impurities in 5 technical batches, DACO: 2.13.3,IIA 1.11.1 CBI
- 1908583 2010, 1st amendment to material accountability of chronic tox sample of fluopyram, DACO: 2.13.3,IIA 1.11.2 CBI
- 1908588 2010, 1st amendment to material accountability of fluopyram batches used in toxicological and ecotoxicological studies, DACO: 2.13.3,IIA 1.11.2 CBI
- 1908589 2010, Fluopyram (AE C656948) - Toxicological equivalence assessment of the technical specification with the material tested in toxicity studies - 1st amendment, DACO: 2.13.3,IIA 1.11.2 CBI
- 1908590 2010, Fluopyram (AE C656948) - Statement on the ecotoxicological assessment of the proposed technical specification, DACO: 2.13.3,IIA 1.11.2
- 1908593 2010, Material accountability of fluopyram (AE C656948) - Re-analysis of impurities in chronic tox sample, DACO: 2.13.3,IIA 1.11.2 CBI
- 1908594 2010, Material accountability of fluopyram batches used in toxicological and ecotoxicological studies - Re-analysis of impurities, DACO: 2.13.3,IIA 1.11.2 CBI
- 1908596 2010, Analytical Method, AE C656948 Impurities in technical grade substance [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI
- 1908597 2010, Validation of [CBI removed] Impurities on technical grade active substance [CBI removed], DACO: 2.13.4,IIA 4.2.3 CBI
- 1908598 2010, Clarification regarding impurities in the material accountability studies of fluopyram, DACO: 2.13.4,IIA 4.2.3 CBI

- 1599620 2006, Analytical method 00973 for the determination of residues of AE C656948 in soil by HPLC-MS/MS, DACO: 8.2.2.1,IIA 4.4
- 1599622 2007, Analytical method 01023 for the determination of residues of AE C656948 and its metabolites [CBI removed] in soil by HPLC-MS/MS, DACO: 8.2.2.1,IIA 4.4
- 1599623 2007, Analytical method 01051 for the determination of fluopyram (AE C656948) in drinking and surface water by HPLC-MS/MS, DACO: 8.2.2.3,IIA 4.5
- 1599625 2008, Analytical Method 01068 for the determination of residues of AE C656948 in soil by HPLC-MS/MS, DACO: 8.2.2.1,IIA 4.4
- 1599627 2008, Analytical method for the determination of residues of AE C656948 and its metabolites AE C656948-benzamide, AE C656948-7-hydroxy, and AE C656948-PCA in soil and sediment using LC/MS/MS, DACO: 8.2.2.2,IIA 4.6
- 1599642 2008, Determination of fluopyram (AE C656948) in water by LC/MS/MS, DACO: 8.2.2.3,IIA 4.5
- 1599766 2008, Independent laboratory validation of analytical method 01023 for the determination of residues of AE C656948 and its metabolites AE C656948-benzamide (AE F148815), AE C656948-7-hydroxy (BCS-AA-10065) and AE C656948-PCA in soil by HPLC-MS/MS on soil
- 1599767 2008, Independent laboratory validation of analytical method 01051 for the determination of fluopyram (AE C656948) in drinking and surface water by HPLC-MS/MS, DACO: 8.2.2.3,IIA 4.5
- 1599279 2008, Composition statement - Plant protection product - Fluopyram SC 500 (500 g/L), DACO: 3.3.2,IIIA 1.4.1 CBI
- 1599280 2008, Product chemistry of fluopyram 500 SC, DACO: 3.2.1,3.3.1,3.3.2,IIIA 1.4.2 CBI
- 1599283 2008, Manufacturing process description for fluopyram 500 SC, DACO: 3.2.2,IIIA 1.4.5.1 CBI
- 1599304 2008, Physical, chemical and technical properties of fluopyram SC 500 (500 g/L), DACO: 3.5.1,3.5.2,3.5.3,3.5.6,3.5.7,3.5.9,3.7,8.2.2.1,8.2.3.6,IIIA 2.1,IIIA 2.4.2,IIIA 2.5.1,IIIA 2.5.2,IIIA 2.5.3,IIIA 2.6.1,IIIA 2.8.2,IIIA 2.8.3.1,IIIA 2.8.3.2,IIIA 2.8.5.
- 1599305 2008, Miscibility of fluopyram 500 SC, DACO: 3.5.13,IIIA 2.11
- 1599306 2008, Dielectric breakdown voltage of fluopyram 500 SC, DACO: 3.5.15,IIIA 2.12
- 1599307 2007, Storage stability of fluopyram SC 500 (500 g/L) - [Packaging material: HDPE] - Interim report (8 weeks), DACO: 3.5.10,3.5.14,IIIA 2.13,IIIA 2.7.1,IIIA 2.7.2,IIIA 2.7.3,IIIA 2.7.4,IIIA 2.7.5
- 1599308 2008, Container material of fluopyram SC 500, DACO: 3.5.5,IIIA 2.14
- 1599309 2008, Safety relevant technical properties of fluopyram SC 500 g/L -Final report-, DACO: 3.5.11,3.5.12,3.5.8,IIIA 2.2.1,IIIA 2.2.2,IIIA 2.3.1,IIIA 2.3.3
- 1599312 2006, Determination of AE C656948 in formulations - Assay - GLC, internal standard, DACO: 3.4.1,IIIA 5.2.1
- 1599313 2008, Validation of GLC-method AM005005MF1 -determination of AE C656948 in formulations-, DACO: 3.4.1,IIIA 5.2.1
- 1599314 2008, Validation of GLC-method AM005005MF1 - Determination of AE C656948 in formulations, DACO: 3.4.1,IIIA 5.2.1
- 1764319 2009, Discussion of the Formation of impurities of Fluopyram 500 SC, DACO: 3.2.3 CBI

- 1983757 2009, Storage stability data of fluopyram SC 500 (500 g/L) - packaging material: HDPE, DACO: 3.5.10,3.5.14 CBI
- 1670065 2008, Composition statement - Plant protection product - Fluopyram + pyrimethanil SC 500 (125 + 375 g/L), DACO: 3.3.2,IIIA 1.4.1 CBI
- 1670068 2008, Product chemistry of fluopyram + pyrimethanil 500 SC, DACO: 3.2.2,IIIA 1.4.5.1 CBI
- 1670069 2008, Discussion of the formation of impurities of fluopyram & pyrimethanil - SC 500 (125 + 375 g/L), DACO: 3.2.3,IIIA 1.4.5.2 CBI
- 1670071 2008, Physical and chemical properties of fluopyram + pyrimethanil 500 SC, DACO: 3.5.1,3.5.2,3.5.3,3.5.6,3.5.7,3.5.9,IIIA 2.1,IIIA 2.4.2,IIIA 2.5.2,IIIA 2.6.1
- 1670072 2008, Miscibility of fluopyram & pyrimethanil - SC 500 (125+ 375 g/L), DACO: 3.5.13,IIIA 2.11
- 1670073 2008, Dielectric breakdown voltage of fluopyram & pyrimethanil - SC 500 (125+ 375 g/L), DACO: 3.5.15,IIIA 2.12
- 1670074 2008, Container material of fluopyram & pyrimethanil - SC 500 (125+ 375 g/L), DACO: 3.5.5,IIIA 2.14
- 1670075 2008, Determination of safety-relevant data of fluopyram + pyrimethanil SC 500 (125+375 g/L), DACO: 3.5.11,3.5.12,3.5.8,IIIA 2.2.1,IIIA 2.2.2,IIIA 2.3.1,IIIA 2.3.3
- 1670078 2008, Determination of fluopyram and pyrimethanil in formulations - assay - GLC, internal standard, DACO: 3.4.1,IIIA 5.2.1,IIIA 5.2.2
- 1670079 2008, Validation of GLC-method AM010007MF1 - determination of fluopyram and pyrimethanil in formulations, DACO: 3.4.1,IIIA 5.2.1,IIIA 5.2.2
- 1838560 2009, Determination of pH of Water, Flowables, and Aqueous Solutions, DACO: 3.5.7 CBI
- 1838561 2008, Brookfield Viscosity, DACO: 3.5.9 CBI
- 1838565 2009, Storage Stability Data of fluopyram + pyrimethanil SC 500 (125+375 g/L), DACO: 3.5.10,3.5.14 CBI
- 1670779 2008, Product chemistry of fluopyram + prothioconazole 400 SC, DACO: 3.2.2,3.3.1,3.3.2,3.4.1,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.15,3.5.2,3.5.3,3.5.6,3.5.7,3.5.8,3.5.9,IIIA 1.4.1,IIIA 1.4.2,IIIA 1.4.5.1,IIIA 2.1,IIIA 2.11,IIIA 2.12,IIIA 2.2.1,IIIA 2.2.2
- 1670784 2008, Container material of fluopyram & prothioconazole - SC 400 (200 + 200 g/L), DACO: 3.5.5,IIIA 2.14
- 1838577 2009, Determination of pH of Water, Flowables, and Aqueous Solutions, DACO: 3.5.7 CBI
- 1838578 2008, Brookfield Viscosity, DACO: 3.5.9 CBI
- 2174226 2012, Storage Stability and Corrosion Characteristics of Fluopyram + Prothioconazole SC 400 (Propulse 400 SC), DACO: 3.5.10,3.5.14 CBI

## 2.0 Human and Animal Health

| PMRA Document Number | Reference                                                                                                                                                                                                                                                                           |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1599505              | 2003, 28-day toxicity study in the rat by dietary administration Code: AE 1344122, DACO: 4.8,IIA 5.8                                                                                                                                                                                |
| 1599513              | 2008, [Phenyl-UL-14C]AE 656948: Absorption, distribution, excretion and metabolism in the rat, DACO: 4.5.9,IIA 5.1.1                                                                                                                                                                |
| 1599517              | 2008, [Phenyl-UL-14C]AE C656948: Distribution of the total radioactivity in male and female rats determined by quantitative whole body autoradiography (QWBA), determination of the exhaled <sup>14</sup> CO <sub>2</sub> and metabolic profiling in excreta, DACO: 4.5.9,IIA 5.1.1 |
| 1599524              | 2008, [Pyridyl-2,6-14C]AE C656948 - Metabolism in organs and tissues of male and female rats (three timepoints), DACO: 4.5.9,IIA 5.1.1                                                                                                                                              |
| 1599526              | 2008, [Pyridyl-2,6-14C]AE C656948: Absorption, distribution, excretion and metabolism in the rat, DACO: 4.5.9,IIA 5.1.1                                                                                                                                                             |
| 1599529              | 2008, [Pyridyl-2,6-14C]AE C656948: Distribution of the total radioactivity in male and female rats determined by quantitative whole body autoradiography (QWBA), determination of the exhaled <sup>14</sup> CO <sub>2</sub> , DACO: 4.5.9,IIA 5.1.1                                 |
| 1599533              | 2007, A subacute dermal toxicity study in rats with technical grade AE C656948, DACO: 4.3.5,IIA 5.3.7                                                                                                                                                                               |
| 1599534              | 2008, A subchronic neurotoxicity screening study with technical grade AE C656948 in Wistar rats, DACO: 4.5.13,IIA 5.7.4                                                                                                                                                             |
| 1599545              | 2003, Acute toxicity in the rat after oral administration AE 1344122 Project AE C638206, DACO: 4.8,IIA 5.8                                                                                                                                                                          |
| 1599547              | 2003, AE 1344122 (metabolite of AE C638206): Induction of chromosome aberrations in cultured human peripheral blood lymphocytes, DACO: 4.8,IIA 5.8                                                                                                                                  |
| 1599548              | 2008, AE C656948 - Chronic toxicity study in the dog by dietary administration, DACO: 4.3.2,IIA 5.3.4                                                                                                                                                                               |
| 1599551              | 2008, AE C656948 (fluopyram) - In vitro studies on the potential interactions with thyroid peroxidase-catalyzed reactions, DACO: 4.8,IIA 5.5.4                                                                                                                                      |
| 1599552              | 2007, AE C656948 (project: AE C656948) - In vitro chromosome aberration test with Chinese hamster V79 cells, DACO: 4.5.6,IIA 5.4.2                                                                                                                                                  |
| 1599553              | 2008, AE C656948 (project: fluopyram) - Salmonella/microsome test - Plate incorporation and preincubation method, DACO: 4.5.4,IIA 5.4.1                                                                                                                                             |
| 1599555              | 2008, AE C656948 - 90-day toxicity study in the dog by dietary administration, DACO: 4.3.2,IIA 5.3.3                                                                                                                                                                                |
| 1599556              | 2008, AE C656948 - 90-day toxicity study in the mouse by dietary administration, DACO: 4.3.1,IIA 5.3.2                                                                                                                                                                              |
| 1599557              | 2007, AE C656948 - 90-day toxicity study in the rat by dietary administration, DACO: 4.3.1,IIA 5.3.2                                                                                                                                                                                |
| 1599558              | 2007, AE C656948 - Acute eye irritation on rabbits, DACO: 4.2.4,IIA 5.2.5                                                                                                                                                                                                           |
| 1599559              | 2007, AE C656948 - Acute inhalation toxicity in rats, DACO: 4.2.3,IIA 5.2.3                                                                                                                                                                                                         |
| 1599561              | 2007, AE C656948 - Acute skin irritation/corrosion on rabbits, DACO: 4.2.5,IIA 5.2.4                                                                                                                                                                                                |

- 1599563 2007, AE C656948 - Acute toxicity in the rat after dermal application, DACO: 4.2.2,IIA 5.2.2
- 1599564 2007, AE C656948 - Acute toxicity in the rat after oral administration, DACO: 4.2.1,IIA 5.2.1
- 1599571 2008, AE C656948 - Developmental toxicity study in the rabbit by gavage, DACO: 4.5.3,IIA 5.6.11
- 1599573 2008, AE C656948 - Evaluation of potential dermal sensitization in the local lymph node assay in the mouse, DACO: 4.2.6,IIA 5.2.6
- 1599574 2008, AE C656948 - Exploratory 28-day toxicity study in the rat by dietary administration, DACO: 4.3.3,IIA 5.3.1
- 1599576 2008, AE C656948 - Mechanistic 14-day toxicity study in the mouse by dietary administration (hepatotoxicity and thyroid hormone investigations), DACO: 4.8,IIA 5.5.4
- 1599577 2007, AE C656948 - Micronucleus-test on the male mouse, DACO: 4.5.7,IIA 5.4.4
- 1599578 2008, AE C656948 - Preliminary 28-day toxicity study in the dog by gavage, DACO: 4.3.3,IIA 5.3.1
- 1599579 2008, AE C656948 - Preliminary 28-day toxicity study in the mouse by dietary administration, DACO: 4.3.3,IIA 5.3.1
- 1599580 2007, AE C656948 - Salmonela/microsome test plate incorporation and preincubation method, DACO: 4.5.4,IIA 5.4.1
- 1599581 2007, AE C656948 - V79/HPRT-test in vitro the detection of induced forward mutations, DACO: 4.5.5,IIA 5.4.3
- 1599610 2008, AE C656948: Developmental toxicity study in the rat by gavage, DACO: 4.5.2,IIA 5.6.10
- 1599611 2003, AE C657188 (metabolite of AE C638206): Induction of chromosome aberrations in cultured human peripheral blood lymphocytes, DACO: 4.8,IIA 5.8
- 1599612 2008, AE C657188 (PCA) Preliminary 28-day toxicity study in the rat by dietary administration Version 2, DACO: 4.8,IIA 5.8
- 1599613 2003, AE C657188 - V79/HPRT-test in vitro for the detection of induced forward mutations, DACO: 4.8,IIA 5.8
- 1599617 1984, Chen, H. J., Age and sex difference in serum and pituitary thyrotropin concentrations in the rat: influence by pituitary adenoma, Experimental Gerontology, Vol. 19, pp. 1-6, DACO: 4.8,IIA 5.5.4
- 1599618 2007, An acute oral neurotoxicity screening study with technical grade AE C656948 in Wistar rats, DACO: 4.5.12,IIA 5.7.1
- 1599630 2000, Bacterial mutation assay AE C657188 (plant metabolite of AE C638206) Code: AE C657188 00 1B99 0002, DACO: 4.8,IIA 5.8
- 1599631 2008, Boring, C. C.; Squires, T. S.; Tong, T.; Montgomery, S., Cancer statistics, 1994, A Cancer Journal for Clinicians, 44, pp. 7-26, DACO: 4.8,IIA 5.5.4
- 1599632 2008, Carcinogenicity study of AE C656948 in the C57BL/6J mouse by dietary administration, DACO: 4.4.3,IIA 5.5.3
- 1599635 2008, Chronic toxicity and carcinogenicity study of AE C656948 in the Wistar rat by dietary administration, DACO: 4.4.2,4.4.4,IIA 5.5.2
- 1599741 2008, Fluopyram (AE C656948) - 7-day mechanistic study in the female Wistar rat by dietary administration, DACO: 4.8,IIA 5.5.4

- 1599762 2006, Holsapple, M.; Pitot, H. C.; Cohen, S. H.; Boobis, A. R.; Klanig, J. E.; Pastoor, T.; Dellarco, V. L.; Dragan, Y. P., Forum - Mode of action in relevance of rodent liver tumors to human cancer risk, *Toxicological Sciences* 89(1), pp. 51-56, DACO: 4.8,IIA 5.5.4
- 1599763 2003, Moore, J. T.; Moore, L. B.; Maglich, J. M.; Kliewer, S. A., Functional and structural comparison of PXR and CAR, *Biochimica et Biophysica Acta* 1619, pp. 235-238, DACO: 4.8, IIA 5.5.4
- 1599799 1992, Capen, C. C., Pathophysiology of chemical injury of the thyroid gland, *Toxicology Letters*, 64/65, pp. 381-388. DACO: 4.8,IIA 5.5.4
- 1599800 2000, Kelly, G., Peripheral metabolism of thyroid hormones: A Review, *Alternative Medicine Review*, 5(4), pp. 306-333, DACO: 4.8,IIA 5.5.4
- 1599802 2008, Phenobarbital - 7-day mechanistic study in the female Wistar rat by gavage, DACO: 4.8,IIA 5.5.4
- 1599803 2008, Phenobarbital - Mechanistic 14-day toxicity study in the mouse by oral gavage (hepatotoxicity and thyroid hormone investigations), DACO: 4.8,IIA 5.5.4
- 1599804 1996, Whysner, J.; Ross, P. M.; Williams, G. M., Phenobarbital mechanistic data and risk assessment: Enzyme induction, enhanced cell proliferation, and tumor promotion, *Pharmacol. Ther.*, 71(1/2), pp. 153-191, DACO: 4.8,IIA 5.5.4
- 1599809 2000, Rat acute oral toxicity AE C657188 (plant metabolite of AE C638206) Code: AE C657188 00 1B99 0002, DACO: 4.8,IIA 5.8
- 1599812 1998, Hill, R. N.; Crisp, T. M.; Hurley, P. M.; Rosenthal, S. L.; Singh, D. V., Risk assessment of thyroid follicular cell tumors, *Environmental Health Perspectives*, 106(8), DACO: 4.8,IIA 5.5.4
- 1599813 2003, Salmonella/microsome test - Plate incorporation and preincubation method Code: AE 1344122, DACO: 4.8,IIA 5.8
- 1599815 2001, Anon., Some thyrotropic agents - Summary of data reported and evaluation, DACO: 4.8, IIA 5.5.4
- 1599823 2008, Technical grade AE C656948: A dose range-finding reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599824 2008, Technical grade AE C656948: A two generation reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599826 2008, Technical grade AE C656948: A two generation reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599827 2008, Technical grade AE C656948: A two generation reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599828 2008, Technical grade AE C656948: A two generation reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599829 2008, Technical grade AE C656948: A two generation reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599830 2008, Technical grade AE C656948: A two generation reproductive toxicity study in the Wistar rat, DACO: 4.5.1,IIA 5.6.1
- 1599831 1991, Curran, P. G.; DeGroot, L. J., The effect of hepatic enzyme-inducing drugs on thyroid hormones and the thyroid gland, *Endocrine Reviews*, 12(2), pp. 135-150, DACO: 4.8,IIA 5.5.4
- 1599832 1989, McClain, R. M.; Levin, A. A.; Posch, R.; Downing, J. C., The effect of phenobarbital on the metabolism and excretion of Thyroxine in rats, *Toxicology and Applied Pharmacology*, 99, pp. 216-228, DACO: 4.8,IIA 5.5.4

- 1599870 2003, V79/HPRT-test in vitro for the detection of induced forward mutations  
Code: AE 1344122 (metabolite of AE C628206), DACO: 4.8,IIA 5.8
- 1654271 1973, Bastomsky, C. H., The biliary excretion of thyroxine and its glucuronic acid  
conjugate in normal and gunn rats, Endo. 92(1), pp. 35-40, DACO: 4.8,IIA 5.5.4
- 1654272 2008, AE C656948 - Mechanistic 3-day toxicity study in the male mouse  
(pharmacokinetic investigations of the clearance of intravenously administered  
125I-thyroxine), DACO: 4.8,IIA 5.5.4
- 1654273 2008, AE C656948 - Mechanistic 3-day toxicity study in the male mouse (QPCR  
investigations of gene transcripts in the liver), DACO: 4.8,IIA 5.5.4
- 1661145 2008, AE C656948 - Mechanistic 3-day toxicity study in the male mouse  
(pharmacokinetic investigations of the clearance of intravenously administered  
125I-thyroxine), DACO: 4.8,IIA 5.5.4
- 1661146 2008, AE C656948 - Mechanistic 3-day toxicity study in the male mouse (QPCR  
investigations of gene transcripts in the liver), DACO: 4.8,IIA 5.5.4
- 1729272 2009, AE C656948 Definitive Mechanistic 4-Day Toxicity Study in the Male  
Mouse (Pharmacokinetic Investigations of the Clearance of Interavenously  
Administered 125I\_Thyroxine), DACO: 4.8
- 1764323 2009, Fluopyram (AE C656948) Responses to the February 23, 2009 question  
form Germany BfR on metabolism and toxicology, DACO: 4.8,6.4
- 1764325 2009, Regulatory Position Paper Fluopyram: Response to PMRA on the in-house  
background incidence of "gall bladder absent" in the New Zealand White Rabbit  
fetus, DACO: 4.8
- 1764326 2009, Fluopyram (AE C656948) Weight of evidence evaluation of thyroid  
carcinogenesis in mice and liver carcinogenesis in rats using the IPCS mode of  
action framework, DACO: 4.8
- 1764327 2009, Hexyl Cinnamaldehyde (HCA), Potassium Dichromate (PDC) and  
Formaldehyde (FRM) Evaluation of Potential Dermal Sensitization in the Local  
Lymph Node Assay in the Mouse, DACO: 4.2.9
- 1764328 2008, AE 1801486: Evaluation of potential dermal sensitization in the local lymph  
node assay in the mouse, DACO: 4.2.9
- 1599345 2007, AE C656948: Comparative in vitro dermal absorption study in SC 500  
formulation using human and rat skin, November 30, 2007. SA 07123, M-295237-  
01, ASB2008-5188, DACO 5.8, IIIA 7.6.2
- 1674473 2008, Fluopyram (AE C656948) SC 500 in vivo dermal absorption study in the  
male rat. August 26, 2008. SA 08082, Lynx-PSI N° TXGMP025, ASB2008-8225,  
DACO 5.8, IIIA 7.6.1
- 1599584 2008, AE C656948 500 SC - Magnitude of the residue on grape processed  
commodities, DACO: 7.4.5,IIA 6.5.3
- 1599586 2008, AE C656948 500 SC - Magnitude of the residue on small fruit vine  
climbing subgroup 13F, except fuzzy kiwifruit, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1599587 2008, AE C656948 500 SC: Magnitude of the residue in/on low growing berry  
(crop subgroup 13G), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.2
- 1599619 2008, An analytical method for the determination of residues of AE C656948 in  
crop matrices using LC/MS/MS, DACO: 7.2.1,7.2.4,7.2.5,8.2.2.4,IIA 4.3
- 1599621 2008, Analytical method 00984 for the determination of residues of AE C656948  
and its metabolites (AE F148815, AE C657188, BCS-AA10139, BCS-AA10065  
and AE 1344122) and tebuconazole in/on plant material by HPLC-MS/MS,  
DACO: 7.2.1,7.2.4,7.2.5,8.2.2.4,IIA 4

- 1599624 2008, Analytical method 01061 for the determination of residues of fluopyram (AE C656948) and its metabolites AE F148815, BCS AA 10627 and BCS AA 10650 in/on animal tissues, milk and eggs by HPLC-MS/MS, DACO: 7.2.1,7.2.4,8.2.2.4,IIA 4.3
- 1599626 2008, Analytical method 01079 for the determination of residues of fluopyram (AE C656948) and AE F148815 in/on animal tissues, eggs and milk by HPLC-MS/MS, DACO: 7.2.1,7.2.2,7.2.4,8.2.2.4,IIA 4.3
- 1599645 2008, Determination of the residues of AE C656948 in/on grape (bunch of grapes) and bunch of grapes for wine proc. and the processed fractions (juice; raw juice; washings; pomace, dried; pomace, wet; berry, washed; retentate; pomace, grape; must; wine at 1<sup>st</sup> taste test; wine) after low-volume spraying of AE C656948 (500 SC) in the field in Southern France, DACO 7.4.5, IIA 6.5.3
- 1599646 2008, Determination of the residues of AE C656948 in/on grape (bunch of grapes) and bunch of grapes for wine proc. and the processed fractions (juice; raw juice; washings; pomace, dried; pomace, wet; berry, washed; retentate; pomace, grape; must; wine at 1<sup>st</sup> taste test; wine) after low-volume spraying of AE C656948 (500 SC) in the field in Southern France, DACO 7.4.5, IIA 6.5.3
- 1599658 2008, Determination of the residues of AE C656948 in/on strawberry fruit and the processed fractions (fruit, washed; preserve; washings; jam) after spraying of AE C656948 (500 SC) in the field in Northern France and Belgium, DACO: 7.4.5,IIA 6.5.3
- 1599659 2008, Determination of the residues of AE C656948 in/on strawberry fruit and the processed fractions (fruit, washed; preserve; washings; jam) after spraying of AE C656948 (500 SC) in the field in Southern France and Spain, DACO: 7.4.5,IIA 6.5.3
- 1599660 2008, Determination of the residues of AE C656948 in/on table grape (bunch of grapes) and the processed fractions (raisin; raisin waste; washings) after spraying of AE C656948 (500 SC) in the field in Spain, Portugal, Italy and Greece, DACO: 7.4.5,IIA 6
- 1599737 2008, Extraction efficiency testing of the residue analytical method 00984/M001 for the determination of AE C656948 residues in grapes using aged radioactive residues, DACO: 7.2.1,7.2.4,IIA 4.3
- 1599760 2008, Fluopyram: Feeding Study Laying Hens (*Gallus gallus domesticus*), DACO: 7.5,7.6,IIA 6.4.1
- 1599761 2008, Fluopyram: Feeding study with dairy cows, DACO: 7.5,7.6,IIA 6.4.2
- 1599769 2008, Independent laboratory validation of the analytical method 01079 for the determination of residues of fluopyram (AE C656948) and AE F148815 in/on animal tissues, eggs and milk by HPLC-MS/MS, DACO: 7.2.1,7.2.2,7.2.3,7.2.4,IIA 4.3
- 1599793 2008, Modification M001 of the analytical method 00984 for the determination of residues of AE C656948 and its metabolites (AE F148815, AE C657188 and BCS AA10139) and tebuconazole in/on plant material by LC-MS/MS, DACO: 7.2.1,7.2.4,7.2.5,8.2.2.4,IIA 4.3
- 1599801 2008, Phase report: 6 months stability in orange of study 07-02 - Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188 and BCS-AA10139) in orange during deep freeze storage for up to 24 months, DACO: 7.3,IIA 6.1.1

- 
- 1599821 2008, Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188, BCS-AA10139 and BCS-AA10065) in plants during deep freeze storage for up to 24 months, DACO: 7.3,IIA 6.1.1
- 1784472 2009, Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188, BCS-AA10139 and BCS-AA10065) in plants during deep freeze storage for up to 36 months - Progress interim report, DACO: 7.3
- 1804905 2009, Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188 and BCS-AA10139) in orange during deep freeze storage for up to 36 months - Progress interim report (Phase Report: 24 months stability in orange of study 07-02), DACO 7.3
- 1599640 2008, Degradation of [phenyl-UL-14C] and [pyridyl-2,6-14C]AE C656948 by plant suspension cell cultures, DACO: 6.3,IIA 6.2.1
- 1599779 2007, Metabolism of [phenyl-UL-14C]AE C656948 in beans after spray application, DACO: 6.3,IIA 6.2.1
- 1599780 2008, Metabolism of [phenyl-UL-14C]AE C656948 in confined rotational crops, DACO: 6.3,7.4.4,IIA 6.2.1,IIA 6.6.2
- 1599781 2007, Metabolism of [phenyl-UL-14C]AE C656948 in potatoes, DACO: 6.3,IIA 6.2.1
- 1599782 2008, Metabolism of [phenyl-UL-14C]AE C656948 in red pepper after drip application, DACO: 6.3,IIA 6.2.1
- 1599785 2007, Metabolism of [phenyl-UL14C]AE C656948 in grapes after spray application, DACO: 6.3,IIA 6.2.1
- 1599786 2007, Metabolism of [pyridyl-2,6-14C]AE C656948 in grapes after spray application, DACO: 6.3,IIA 6.2.1
- 1599787 2008, Metabolism of [pyridyl-2,6-14C]AE C656948 in beans after spray application, DACO: 6.3,IIA 6.2.1
- 1599788 2008, Metabolism of [pyridyl-2,6-14C]AE C656948 in confined rotational crops, DACO: 6.3,7.4.4,IIA 6.2.1,IIA 6.6.2
- 1599789 2007, Metabolism of [pyridyl-2,6-14C]AE C656948 in potatoes, DACO: 6.3,IIA 6.2.1
- 1599790 2008, Metabolism of [pyridyl-2,6-14C]AE C656948 in red pepper after drip application, DACO: 6.3,IIA 6.2.1
- 1599783 2008, Metabolism of [phenyl-UL-14C]AE C656948 in the lactating goat, DACO: 6.2,IIA 6.2.3
- 1599784 2008, Metabolism of [phenyl-UL-14C]AE C656948 in the laying hen, DACO: 6.2,IIA 6.2.2
- 1599791 2008, Metabolism of [pyridyl-2,6-14C]AE C656948 in the lactating goat, DACO: 6.2,IIA 6.2.3
- 1599792 2008, Metabolism of [pyridyl-2,6-14C]AE C656948 in the laying hen, DACO: 6.2,IIA 6.2.2
- 1983731 2010, Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188, BCS-AA10139 and BCS-AA10065) in plants during deep freeze storage for up to 36 months, DACO: 7.3
- 1983732 2010, Storage stability of residues of AE C656948 and its metabolites (AE F148815, AE C657188 and BCS-AA10139) in orange during deep freeze storage for up to 36 months, DACO: 7.3
- 1654363 2008, AE C656948 500 SC - Magnitude of the residue in/on crop tuberous and corm vegetables (crop subgroup 1C), DACO: IIA 6.3.8
-

- 1654364 2008, AE C656948 500 SC - Magnitude of the residue in/on sugar beets and leaves of root and tuber vegetables (crop group 2), DACO: IIA 6.3.10, IIA 6.3.9
- 1654372 2008, AE C656948 500 SC - Magnitude of the residue in/on peanut processed commodities, DACO: 7.4.5, IIA 6.5.3
- 1654373 2008, AE C656948 500 SC - Magnitude of the residue in/on field corn processed commodities and aspirated grain fractions, DACO: 7.4.5, IIA 6.5.3
- 1654374 2008, AE C656948 500 SC - Magnitude of the residue in/on wheat processed commodities and aspirated grain fractions, DACO: 7.4.5, IIA 6.5.3
- 1654375 2008, AE C656948 500 SC - Magnitude of the residue in/on soybean processed commodities and aspirated grain fractions, DACO: 7.4.5, IIA 6.5.3
- 1654376 2008, AE C656948 500 SC - Magnitude of the residue in/on cotton processed commodities, DACO: 7.4.5, IIA 6.5.3
- 1654378 2008, AE C656948 500 SC: Magnitude of the residue in/on canola processed commodities, DACO: 7.4.5, IIA 6.5.3
- 1654379 2008, AE C656948 500 SC - Magnitude of the residue in/on sugar beet processed commodities, DACO: 7.4.5, IIA 6.5.3
- 1654380 2008, AE C656948 500 SC - Magnitude of the residue in/on potato processed commodities, DACO: 7.4.5, IIA 6.5.3
- 1654383 2007, AE C656948 500 SC - Magnitude of the residue on apple processed commodities, DACO: 7.4.5, IIA 6.5.3
- 1654391 2007, Determination of the residues of AE C656948 in/on winter rape and summer rape and the processed fractions (oil, refined; oil, screwpressed; crude oil; ...) after spraying of AE C656948 (500 SC) in the field in Southern France and Italy, DACO: 7.4
- 1654393 2007, Determination of the residues of AE C656948 in/on apple fruit and the processed fractions (fruit, washed; raw sauce; sauce; washings; strain rest; juice; pomace, wet; pomace, dried; raw juice; fruit, dried, peel rest; fruit, peeled) after spraying of AE C656948 (500 SC) in the field in Southern France and Italy, DACO 7.4.5, IIA 6.5.3
- 1654394 2007, Determination of the residues of AE C656948 in/on apple fruit and the processed fractions (fruit, washed; raw sauce; sauce; washings; strain rest; juice; pomace, wet; pomace, dried; raw juice; fruit, dried, peel rest; fruit, peeled) after spraying of AE C656948 (500 SC) in the field in Belgium and the United Kingdom, DACO 7.4.5, IIA 6.5.3
- 1654395 2007, Determination of the residues of AE C656948 in/on winter rape seed and the processed fractions (oil, refined; oil, screwpressed; crude oil; extracted meal; oil, solv. extracted; pomace) after spraying of AE C656948 (500 SC) in the field in, Germany, DACO 7.4.5, IIA 6.5.3
- 1654399 2008, AE C656948 500 SC - Magnitude of the residue in cotton (rotational crop tolerance), DACO: 7.4.4, IIA 6.6.3
- 1654400 2008, AE C656948 500 SC - Magnitude of the residue in field rotational crops (240-day plant back interval), DACO: 7.4.4, IIA 6.6.3
- 1654401 2008, AE C656948 500 SC - Magnitude of the residue in alfalfa (rotational crop tolerance), DACO: 7.4.4, IIA 6.6.3
- 1661215 2008, AE C656948 500 SC - Magnitude of the residue in/on dried, shelled peas and beans and the foliage of legume vegetables (crop subgroups 6C and 7A), DACO: 7.4.1, 7.4.2, 7.4.6, IIA 6.3.1

- 
- 1661216 2008, AE C656948 500 SC - Magnitude of the residue in/on soybean, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661219 2008, AE C656948 500 SC - Magnitude of the residue in/on cucurbit vegetables (crop group 9), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661222 2008, AE C656948 500 SC - Magnitude of the residue in/on pome fruit (CG 11), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661231 2008, AE C656948 500 SC - Magnitude of the residue on stone fruit, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661238 2008, AE C656948 500 SC - Magnitude of the residue on tree nuts, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661247 2008, AE C656948 500 SC - Magnitude of the residue in/on wheat and sorghum (as part of crop groups 15 and 16, expect rice), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661248 2008, AE C656948 500 SC - Magnitude of the residue in/on field corn and sweet corn (as part of crop groups 15 and 16, expect rice), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661252 2008, AE C656948 500 SC - Magnitude of the residue in/on peanuts, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661254 2008, AE C656948 500 SC - Magnitude of the residue in/on canola, DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661260 2008, AE C656948 500 SC - Magnitude of the residue in/on bananas (import tolerance), DACO: 7.4.1,7.4.2,7.4.6,IIA 6.3.1
- 1661266 2008, AE C656948 500 SC - Magnitude of the residue in/on crop tuberous and corm vegetables (crop subgroup 1C), DACO: IIA 6.3.8
- 1661267 2008, AE C656948 500 SC - Magnitude of the residue in/on sugar beets and leaves of root and tuber vegetables (crop group 2), DACO: IIA 6.3.10,IIA 6.3.9
- 1661275 2008, AE C656948 500 SC - Magnitude of the residue in/on peanut processed commodities, DACO: 7.4.5,IIA 6.5.3
- 1661276 2008, AE C656948 500 SC - Magnitude of the residue in/on field corn processed commodities and aspirated grain fractions, DACO: 7.4.5,IIA 6.5.3
- 1661280 2008, AE C656948 500 SC - Magnitude of the residue in/on wheat processed commodities and aspirated grain fractions, DACO: 7.4.5,IIA 6.5.3
- 1661282 2008, AE C656948 500 SC - Magnitude of the residue in/on soybean processed commodities and aspirated grain fractions, DACO: 7.4.5,IIA 6.5.3
- 1661283 2008, AE C656948 500 SC - Magnitude of the residue in/on cotton processed commodities, DACO: 7.4.5,IIA 6.5.3
- 1661285 2008, AE C656948 500 SC: Magnitude of the residue in/on canola processed commodities, DACO: 7.4.5,IIA 6.5.3
- 1661286 2008, AE C656948 500 SC - Magnitude of the residue in/on sugar beet processed commodities, DACO: 7.4.5,IIA 6.5.3
- 1661287 2008, AE C656948 500 SC - Magnitude of the residue in/on potato processed commodities, DACO: 7.4.5,IIA 6.5.3
- 1661291 2007, AE C656948 500 SC - Magnitude of the residue on apple processed commodities, DACO: 7.4.5,IIA 6.5.3
- 1661299 2008, AE C656948 500 SC - Magnitude of the residue in cotton (rotational crop tolerance), DACO: 7.4.4,IIA 6.6.3
- 1661301 2008, AE C656948 500 SC - Magnitude of the residue in field rotational crops (240-day plant back interval), DACO: 7.4.4,IIA 6.6.3
-

- 1661302 2008, AE C656948 500 SC - Magnitude of the residue in alfalfa (rotational crop tolerance), DACO: 7.4.4,IIA 6.6.3
- 1921416 2010, Fluopyram Projected Percent Crop Treated, DACO: 10.7.2 CBI
- 1921417 2010, Fluopyram Projected Percent Crop Treated, DACO: 10.7.2
- 1922911 2010, Projections of Percent crop Treated with fluopyram products in Canada, DACO: 10.7.2 CBI
- 1670088 2008, AE C656948 500 SC - Magnitude of the residue in/on pome fruit (CG 11), DACO: 7.4.1,9.3.2,IIA 8.3.1.1

### 3.0 Environment

| PMRA Document Number | Reference                                                                                                                                                                                                                                                                                             |
|----------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1599766              | 2008, Independent laboratory validation of analytical method 01023 for the determination of residues of AE C656948 and its metabolites AE C656948-benzamide (AE F148815), AE C656948-7-hydroxy (BCS-AA-10065) and AE C656948-PCA in soil by HPLC-MS/MS on soil, DACO: 8.2.2.1,8.2.2.2,IIA 4.4,IIA 4.6 |
| 1599620              | 2006, Analytical method 00973 for the determination of residues of AE C656948 in soil by HPLC-MS/MS, DACO: 8.2.2.1,IIA 4.4                                                                                                                                                                            |
| 1599622              | 2007, Analytical method 01023 for the determination of residues of AE C656948 and its metabolites AE C656948-benzamide (AE F148815), AE C656948-7-hydroxy (BCS-AA-10065) and AE C656948-PCA in soil by HPLC-MS/MS, DACO: 8.2.2.1,IIA 4.4                                                              |
| 1599625              | 2008, Analytical Method 01068 for the determination of residues of AE C656948 in soil by HPLC-MS/MS, DACO: 8.2.2.1,IIA 4.4                                                                                                                                                                            |
| 1599627              | 2008, Analytical method for the determination of residues of AE C656948 and its metabolites AE C656948-benzamide, AE C656948-7-hydroxy, and AE C656948-PCA in soil and sediment using LC/MS/MS, DACO: 8.2.2.2,IIA 4.6                                                                                 |
| 1599623              | 2007, Analytical method 01051 for the determination of fluopyram (AE C656948) in drinking and surface water by HPLC-MS/MS, DACO: 8.2.2.3,IIA 4.5                                                                                                                                                      |
| 1599642              | 2008, Determination of fluopyram (AE C656948) in water by LC/MS/MS, DACO: 8.2.2.3,IIA 4.5                                                                                                                                                                                                             |
| 1599767              | 2008, Independent laboratory validation of analytical method 01051 for the determination of fluopyram (AE C656948) in drinking and surface water by HPLC-MS/MS, DACO: 8.2.2.3,IIA 4.5                                                                                                                 |
| 1599507              | 2007, [14C]-AE C656948: Aqueous hydrolysis at pH 4, 7 and 9, DACO: 8.2.3.2,IIA 2.9.1,IIA 7.5                                                                                                                                                                                                          |
| 1599609              | 2007, AE C656948: Determination of the quantum yield and assessment of the environmental half-life of the direct photodegradation in water, DACO: 8.2.3.3,8.2.3.3.2,IIA 2.9.3,IIA 2.9.4,IIA 7.6                                                                                                       |
| 1599510              | 2008, [Phenyl-UL-14C]AE C656948 and [pyridyl-2,6-14C]AE C656948: Phototransformation in natural water, DACO: 8.2.3.3,8.2.3.3.2,IIA 2.9.4,IIA 7.6                                                                                                                                                      |
| 1599509              | 2007, [14C]-AE C656948: Soil photolysis, DACO: 8.2.3.3.1,IIA 7.1.3                                                                                                                                                                                                                                    |
| 1599508              | 2008, [14C]-AE C656948: Aqueous photolysis in buffer at pH 7, DACO: 8.2.3.3.2,IIA 2.9.2,IIA 7.6                                                                                                                                                                                                       |

- 1599608 2007, AE C656948: Calculation of the chemical lifetime in the troposphere, DACO: 8.2.3.3.3,IIA 2.10,IIA 7.10
- 1599516 2008, [Phenyl-UL-14C]AE C656948: Aerobic soil metabolism/degradation and time-dependent sorption in four soils, DACO: 8.2.3.4.2,8.2.4.2,IIA 7.1.1,IIA 7.2.1,IIA 7.2.3,IIA 7.4.1
- 1599527 2008, [Pyridyl-2,6-14C]AE C656948: Aerobic metabolism/degradation and time-dependent sorption in soils, DACO: 8.2.3.4.2,8.2.4.2,IIA 7.1.1,IIA 7.2.1,IIA 7.2.3,IIA 7.4.1
- 1599511 2008, [Phenyl-UL-14C] and [pyridyl-2,6-14C]AE C656948: Aerobic soil metabolism in two US soils, DACO: 8.2.3.4.2,IIA 7.1.1,IIA 7.2.1
- 1774640 2009, Fluopyram - Bayer CropScience Response to PMRA Comments Regarding Redox Potential (Eh) in Anaerobic Soil and Aquatic Studies, DACO: 8.2.3.4.4,8.2.3.5.5,8.2.3.5.6,IIA 7.1.2,IIA 7.8.2
- 1599512 2008, [Phenyl-UL-14C] and [pyridyl-2,6-14C]AE C656948: Anaerobic soil metabolism, DACO: 8.2.3.4.4,IIA 7.1.2,IIA 7.2.4
- 1599531 2007, [pyridyl-ring-UL-14C]-AE C656948 and [trifluorobenzamide-ring-UL-14C]-AE C656948 - Aerobic aquatic metabolism, DACO: 8.2.3.5.4,8.2.3.6,IIA 7.8.3
- 1599506 2007, [14C-phenyl-UL]AE C656948: Anaerobic aquatic metabolism, DACO: 8.2.3.5.5,8.2.3.5.6,IIA 7.8.2
- 1599528 2007, [pyridyl-2,6-14C]AE C656948: Anaerobic aquatic metabolism, DACO: 8.2.3.5.5,8.2.3.5.6,IIA 7.8.2
- 1599772 2008, Kinetic evaluation of the aerobic aquatic metabolism of fluopyram (AE C656948) in water/sediment systems using MatLab, DACO: 8.2.3.6,IIA 7.8.3
- 1599607 2007, AE C656948: Adsorption/desorption on five soils, DACO: 8.2.4.2,IIA 7.4.1
- 1599735 2008, Evaluation of the time-dependent sorption of fluopyram (AE C656948) based on laboratory batch equilibrium experiments in 8 soils, DACO: 8.2.4.2,IIA 7.4.1
- 1599520 2007, [Pyridine-2,6-14C] AE C656948-7-hydroxy: Adsorption/desorption on four EU soils, DACO: 8.2.4.2, IIA 7.4.2
- 1599751 2008, Fluopyram - Statement on the pyrolytic behaviour under controlled conditions and on the controlled incineration as a safe means of disposal - AE C656948, DACO: 8.4.1,IIA 3.8.1
- 1599652 2007, Determination of the residues of AE C656948 in/on soil after spraying of AE C656948 (250 SC) in the field in Germany, United Kingdom, Sweden, France, Spain and Italy, DACO: 8.6,IIA 7.3.1
- 1599771 2008, Kinetic evaluation of field dissipation studies after application of fluopyram (AE C656948) in Europe according to FOCUS using KinGui, DACO: 8.6,IIA 7.3.1
- 1599497 2007, 1. Interim Report: Determination of the residues of AE C656948 in/on soil after spraying of AE C656948 (250 SC) in Germany and France, DACO: 8.6,IIA 7.3.3
- 1599606 2008, AE C656948: Acute toxicity to earthworms (*Eisenia fetida*) tested in artificial soil with 5 percent peat, DACO: 9.2.3.1,IIA 8.9.1
- 1599589 2008, AE C656948 SC 500: Effects on survival, growth and reproduction on the earthworm *Eisenia fetida* tested in artificial soil with 5 percent peat, DACO: 9.2.3.1,IIA 8.9.2
- 1599733 2007, Effects of AE C656948 (acute contact and oral) on honey bees (*Apis mellifera* L.) in the laboratory, DACO: 9.2.4.1,9.2.4.2,IIA 8.7.1,IIA 8.7.2

- 1599727 2008, Dose-response toxicity (LR50) of AE C656948 SC 500 to the predatory mite *Typhlodromus pyri* (Scheuten) under laboratory conditions, DACO: 9.2.5,IIA 8.8.1.2
- 1599729 2008, Dose-response toxicity (LR50) of AE C656948 SC 500 to the parasitic wasp *Aphidius rhopalosiphi* (Destefani-Perez) under laboratory conditions, DACO: 9.2.6,IIA 8.8.1.1
- 1599599 2008, AE C656948 tech.: Determination of effects on nitrogen transformation in soil, DACO: 9.2.8,9.2.9,IIA 8.10.1
- 1599593 2008, AE C656948 tech.: Determination of effects on carbon transformation in soil, DACO: 9.2.8,9.2.9,IIA 8.10.2
- 1599541 2007, Acute toxicity of AE C656948 (tech.) to the waterflea *Daphnia magna* in a static laboratory test system, DACO: 9.3.2,IIA 8.3.1.1
- 1599770 2008, Influence of AE C656948 (tech.) on development and reproductive output of the waterflea *Daphnia magna* in a static renewal laboratory test system, DACO: 9.3.3,IIA 8.3.2.1
- 1599592 2008, AE C656948 SC 500A G: Influence on the reproduction of the collembola species *Folsomia candida* tested in artificial soil with 5 % peat, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599594 2008, AE C656948 tech.: Determination of effects on growth of pure cultures of a soil fungus, *Agrocybe aegerita*, on a soil-nutrient medium, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599595 2008, AE C656948 tech.: Determination of effects on growth of pure cultures of a soil fungus, *Cladorrhinum foecundissimum*, on a soil-nutrient medium, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599596 2008, AE C656948 tech.: Determination of effects on growth of pure cultures of a soil fungus, *Mucor circinelloides* var. *griseocyanus*, on a soil-nutrient medium, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599597 2008, AE C656948 tech.: Determination of effects on growth of pure cultures of a soil fungus, *Penicillium simplicissimum*, on a soil-nutrient medium, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599598 2008, AE C656948 tech.: Determination of effects on growth of pure cultures of a soil fungus, *Phytophthora nicotianae*, on a soil-nutrient medium, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599634 2008, Chronic dose-response toxicity (ER50) of AE C656948 SC 500 to the rove beetle *Aleochara bilineata* GYLL. under extended laboratory conditions, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599752 2008, Fluopyram SC 500: Influence on mortality and reproduction on the soil mite species *Hypoaspis aculeifer* tested in artificial soil with 5 % peat, DACO: 9.3.4,9.6.6,9.9,IIA 8.16.1
- 1599603 2007, AE C656948: A 96-hour flow-through acute toxicity test with the saltwater mysid (*Americamysis bahia*), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1
- 1599604 2006, AE C656948: A 96-hour shell deposition test with the eastern oyster (*Crassostrea virginica*), DACO: 9.4.2,9.4.3,9.4.4,IIA 8.11.1
- 1599539 2008, Acute toxicity of AE C656948 (tech.) to fish (*Oncorhynchus mykiss*) under static conditions, DACO: 9.5.2.1,9.5.2.3,IIA 8.2.1.1
- 1599537 2008, Acute toxicity of AE C656948 (tech.) to fish (*Cyprinus carpio*) under static conditions, DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2

- 1599538 2008, Acute toxicity of AE C656948 (tech.) to fish (*Lepomis macrochirus*) under static conditions, DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
- 1599543 2008, Acute toxicity of AE C656948 technical to the fathead minnow (*Pimephales promelas*) under static conditions, DACO: 9.5.2.2,9.5.2.3,IIA 8.2.1.2
- 1599544 2006, Acute toxicity of AE C656948 technical to the sheepshead minnow (*Cyprinodon variegatus*) under static conditions, DACO: 9.5.2.4,IIA 8.11.1
- 1599730 2007, Early-life stage toxicity of AE C656948 (tech.) to fish *Pimephales promelas* , DACO: 9.5.3.1,IIA 8.2.4
- 1599536 2008, Acute oral toxicity for bobwhite quail (*Colinus virginianus*) with AE C656948 techn. a.s., DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
- 1654429 2008, AE C656948 - Acute oral toxicity test (LD50) with the zebra finch (*Taeniopygia guttata*) following OECD draft guideline 223, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
- 1661315 2008, AE C656948 - Acute oral toxicity test (LD50) with the zebra finch (*Taeniopygia guttata*) following OECD draft guideline 223, DACO: 9.6.2.1,9.6.2.2,9.6.2.3,IIA 8.1.1
- 1599554 2007, AE C656948 (tech. a.s.) - 5-day-dietary LC50 for bobwhite quail (*Colinus virginianus*), DACO: 9.6.2.4,9.6.2.5,IIA 8.1.2
- 1599600 2007, AE C656948 techn. a.s. : 5-day-dietary LC50 mallard duck (*Anas platyrhynchos*) , DACO: 9.6.2.5,9.6.2.6,IIA 8.1.3
- 1599605 2008, AE C656948: A reproduction study with the Northern bobwhite, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4
- 1599731 2008, Effect of AE C656948 technical on reproduction of the mallard duck (*Anas platyrhynchos*) , DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4
- 1599732 2008, Effect of AE C656948 technical on reproduction of the northern bobwhite quail, DACO: 9.6.3.1,9.6.3.2,9.6.3.3,IIA 8.1.4
- 1599588 2008, AE C656948 SC 500: Effects on soil litter degradation, DACO: 9.6.6,9.9,IIA 8.16.2
- 1599808 2008, *Pseudokircheriella subcapitata* growth inhibition test with fluopyram-lactame, DACO: 9.8.2,9.8.3,IIA 8.4
- 1599862 2007, Toxicity of AE C656948 technical to the 2007, freshwater diatom *Navicula pelliculosa*, DACO: 9.8.2,9.8.3,IIA 8.4
- 1599863 2007, Toxicity of AE C656948 technical to the blue-green algae *Anabaena flos-aquae*, DACO: 9.8.2,9.8.3,IIA 8.4
- 1599864 2007, Toxicity of AE C656948 technical to the green alga *Pseudokirchneriella subcapitata*, DACO: 9.8.2,9.8.3,IIA 8.4
- 1599865 2007, Toxicity of AE C656948 technical to the saltwater diatom *Skeletonema costatum*, DACO: 9.8.3,IIA 8.11.1
- 1599590 2008, AE C656948 SC 500A G - Effect on the vegetative vigour of ten species of non-target terrestrial plants (Tier 1), DACO: 9.8.4,IIA 8.12
- 1599591 2008, AE C656948 SC 500A G effect on seedling emergence and seedling growth test of ten species of non-target terrestrial plants (Tier 1 and 2), DACO: 9.8.4,IIA 8.12
- 1599734 2008, Evaluation of the pre-emergence (PPI) biological activity of AE C656948 SC 500, DACO: 9.8.4,IIA 8.12
- 1599773 2007, *Lemna gibba* G3 - Growth inhibition test with AE C656948 under static conditions, DACO: 9.8.5,IIA 8.6
- 1599602 2008, AE C656948- Toxicity to bacteria, DACO: 9.9,IIA 8.15

- 1599616 2008, AEC656948 - Toxicity to marine amphipods (*Leptocheirus plumulosus*) during a 10-day sediment exposure, DACO: 9.9,IIA 8.5.1
- 1599614 2008, AEC656948 - Life-cycle toxicity test exposing midges (*Chironomus tentans*) to a test substance applied to sediment under static-renewal conditions following EPA test methods, DACO:
- 1599615 2008, AEC656948 - Toxicity to estuarine amphipods (*Leptocheirus plumulosus*) during a 28-day sediment exposure, DACO: 9.9,IIA 8.5.2
- 1599633 2008, *Chironomus riparius* 28-day chronic toxicity test with fluopyram (tech.) in a water-sediment system using spiked water, DACO: 9.9,IIA 8.5.2

#### 4.0 Value

| PMRA Document Number | Reference                                                                                                                                                                                                                                                                                                                                            |
|----------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1599332              | 2008. Fluopyram 500 SC Fungicide (500 g a.i./L fluopyram) for control of Botrytis bunch rot in grape, botrytis grey mould in strawberry and tomato, and <i>Alternaria solani</i> in tomato, DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4, IIIA 6.1.2, IIIA 6.1.3, IIIA 6.2.1, IIIA 6.3, IIIA 6.4.1, IIIA 6.4.2, IIIA 6.4.3. 322pp. |
| 1670787              | 2008. Fluopyram/Prothioconazole Fungicide for Control of Ascochyta Blight of Lentil and Chickpea, Mycosphaerella Blight of Dried Shelled Pea, and White Mold of Dried Shelled Bean and Pea. DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4. 272pp.                                                                                   |
| 1670080              | 2008. Fluopyram + pyrimethanil 500 SC fungicide (125g a.i./L fluopyram + 375g a.i./L pyrimethanil) for control of listed diseases in grapes and small berries, bulbvegetables, tomatoes, and pome fruit. DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4. 420pp.                                                                      |
| 1674457              | 2008. Fluopyram 500 SC Fungicide for control of listed diseases in horticulture and field crops, DACO: 10.2.3.3, 10.2.3.4, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.4. 851pp.                                                                                                                                                                              |
| 2046958              | 2011. Cover Letter for Fluopyram Clarification request Sub No 2008-4863 efficacy data to add drip irrigation strawberries. DACO: 0.8. 2pp.                                                                                                                                                                                                           |
| 2046960              | 2011. Efficacy data. DACO: 10.5. 5pp.                                                                                                                                                                                                                                                                                                                |
| 2046961              | 2011. Efficacy data. DACO: 10.5. 5pp.                                                                                                                                                                                                                                                                                                                |
| 2046963              | 2011. Efficacy data. DACO: 10.5. 7pp.                                                                                                                                                                                                                                                                                                                |