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Pest Management Regulatory Agency

Santé Canada
Agence de réglementation de la lutte antiparasitaire

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PROPOSED REGISTRATION DECISION

NOVALURON

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FOREWORD

Proposed Decision for Novaluron

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing full registration for the sale and use of technical grade active ingredient novaluron and the end-use product Rimon 10 EC for the control of Colorado potato beetle and European corn borer on potato and codling moth and Oriental fruit moth on apple and pear by foliar application.

Current scientific data from the applicant, scientific reports and information from other regulatory agencies were evaluated to determine if, under the proposed conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

This Proposed Registration Decision is a consultation document[1] that summarizes the science evaluation for novaluron and the reasons for the decision. It also describes risk-reduction measures that will be required to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessment of novaluron.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/p-9.01/281990.html)

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OVERVIEW

Proposed Registration Decision for Novaluron

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing full registration for the sale and use of technical grade active ingredient novaluron and the end-use product Rimon 10EC for control Colorado potato beetle and European corn borer on potato and codling moth and Oriental fruit moth on apple and pear by foliar application.

An evaluation of available scientific information found that, under the approved conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

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 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 conditions or proposed conditions of registration[2]. The Act also requires that products have value[3] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g., children) as well as organisms in the environment (e.g., those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

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2 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/p-9.01/281990.html)

3 "Value" as defined by Subsection 2(1) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/p-9.01/281990.html): "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

Before making a registration decision on Novaluron, the PMRA will consider all comments received from the public in response to this consultation document[4]. The PMRA will then publish a Registration Decision Document[5] on Novaluron, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation section of this consultation document.

What is Novaluron?

Novaluron is an insect growth regulator for control of Colorado potato beetle and European corn borer on potato and codling moth and Oriental fruit moth on apple and pear by foliar application. Novaluron inhibits chitin synthesis, affecting moulting, but does not affect the adult stage after development is completed.

❖ Health Considerations

♦ Novaluron is unlikely to affect your health when used according to label directions

Exposure to Novaluron may occur through diet (food and water) or when handling and applying the product. 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 (e.g., children and nursing mothers). Only those uses where 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 using Novaluron products according to label directions.

Novaluron technical grade active ingredient and the end-use product, Rimon 10EC, caused eye and skin irritation in animals. Because of this, the label statement *Warning Eye and Skin Irritant* is required. Rimon 10EC also caused an immune response when applied to the skin. As a result, the label statement *Potential Skin Sensitizer* is required. Novaluron did not cause cancer in animals and was not genotoxic. There was also no

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4 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/p-9.01/281990.html)

5 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act* (http://laws.justice.gc.ca/en/p-9.01/281990.html)

indication that Novaluron caused damage to the nervous system and there were no effects on reproduction. The first signs of toxicity in animals given daily doses of Novaluron over longer periods of time were indications of damage to red blood cells. The risk assessment protects against these effects 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.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Dietary risk estimates (food and water) revealed that children, adults and seniors will typically consume less than 15.0% of the acceptable daily intake for novaluron. Infants, the subpopulation which would ingest the most novaluron relative to body weight, are expected to eat less than 17.3% of the acceptable daily intake. The dietary intake estimate for females of childbearing age (13 to 49 years old) was about 4.7% of the reference dose, which is not a health concern. Based on these estimates, the chronic dietary risk from novaluron is not a concern for all population sub-groups.

Animal studies revealed no acute health effects. Consequently, a single dose of novaluron is not likely to cause acute health effects in the general population (including infants and children).

The *Food and Drugs Act (FDA)* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for FDA purposes through the evaluation of scientific data under the *Pest Control Products Act (PCPA).* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

On-field residue trials conducted throughout Canada, the United States of America and Europe (France, Spain, Italy and Germany) using an end-use product containing novaluron on apple, pear and potato were sufficient to propose MRLs for the pome fruits crop group, which consists of apple, crabapple, loquat, mayhaw, pear, oriental pear and quince, and the tuberous and corm vegetables crop group consisting of arracaha, arrowroot, Chinese artichokes, Jerusalem artichokes, edible canna, cassava roots, chayote roots, chufa, ginger roots, lerens, potatoes, sweet potato roots, tanier corms, taro corms, turmeric roots, yam bean roots and true yam tubers. The proposed MRLs for novaluron can be found in the *Part B- Science Evaluation* section of this consultation document.

♦ **Occupational risks are not of concern when Rimon 10EC is used according to proposed label directions, which include protective measures**

Pesticide applicators mixing, loading or applying Rimon 10EC, and field workers reentering freshly treated fields, can have direct skin contact with novaluron. For this reason, the label will specify that anyone mixing or loading Rimon 10EC must wear long-sleeved shirt and long pants, footwear, eye protection and gloves. Because of this, and taking into consideration that occupational exposure is expected to be limited as this insecticide is applied up to four times per season, risk to pesticide applicators and workers is not a concern.

♦ **Nonoccupational risks are not of concern provided that directions specified on the label are observed.**

The risk to people who are exposed to novaluron both through diet and through apple picking at pick-your-own commercial operations has been assessed and is not of concern.

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

❖ Environmental Considerations

♦ What Happens When Novaluron is Introduced Into the Environment?

Novaluron is toxic to aquatic invertebrates, and non-target plants. Untreated areas (buffer zones) adjacent to aquatic and terrestrial plant habitats are required for the protection of these organisms.

Novaluron enters the environment when used as an insecticide on potatoes and apples/pears. Novaluron is slightly persistent in soil and sediments. Its major breakdown products are moderately persistent in these environments. Neither novaluron nor its major breakdown products are mobile in soil and, therefore, are not expected to leach into groundwater. Based on its low volatility (vapour pressure and Henry's law constant), novaluron residues are not expected in the air.

Novaluron presents high risks to freshwater and marine aquatic invertebrates, and moderate risk to marine mollusks. There is also some risk to susceptible non-target plant species. Beneficial insects, such as, predatory mites, parasitoid wasps, and honeybees may be temporarily suppressed. Therefore, hazard statements and specific instructions to reduce spray drift to terrestrial insects are provided on the product label. Depending on the type of application equipment, timing of spray, and crop, the buffer zones may vary from 3 to 80 metres for freshwater/estuarine aquatic organisms, and 1 to 30 metres for non-target terrestrial plant species.

❖ Value Considerations

♦ What is the Value of Novaluron?

Novaluron is an insect growth regulator that controls major pests on potato, apple and pear.

Foliar application of novaluron controls Colorado potato beetle and European corn borer on potato and codling moth and Oriental fruit moth on apple and pear. It is compatible with current management practices and crop production systems. Growers are familiar with monitoring techniques to determine if and when applications are needed.

Novaluron is an alternative to insecticides currently registered for control of the same pests on potato, apple and pear. This new chemistry is needed for use against Colorado potato beetle, a major pest of potato, to prevent the development of resistance to currently used insecticides, and to replace older insecticides, such as organophosphates, for control of pests on apple and pear.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk reduction measures to protect human and environmental health. These directions are required by law to be followed.

The key risk reduction measures being proposed on the label of Rimon 10 EC Insecticide 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 having direct skin contact with Rimon 10EC, individuals must wear long-sleeved shirts, long pants, footwear, eye protection and gloves during mixing and loading, clean-up and repair activities. Applicators must wear long-sleeved shirt, long pants and footwear.

- **Environment**

Buffer zones are required to protect aquatic organisms and non-target plants from Rimon 10 EC spray drift. Depending on the type of application equipment, timing of spray, and crop, the buffer zones may vary from 3 to 80 metres for aquatic organisms, and 1 to 30 metres for non-target terrestrial plant species.

Risks to beneficial terrestrial organisms, such as, honeybees, predatory mites, and parasitoid wasps, will be mitigated by use of environmental hazard statements.

Next Steps

Before making a registration decision on novaluron, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Registration Decision Document, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and the Agency's response to these comments.

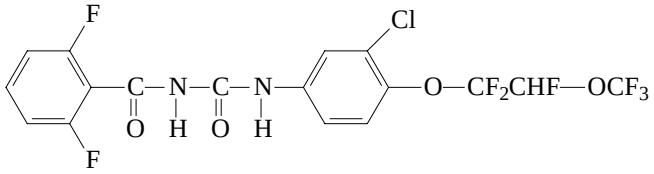
Other Information

At the time the PMRA makes its registration decision, it will publish an Evaluation Report on novaluron (based on the Science Evaluation section of this consultation document). In addition, the test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

SCIENCE EVALUATION

1.0 The Technical Grade Active Ingredient, its Properties and Uses

1.1 Identity of the Technical Grade Active Ingredient

Active substance	Novaluron
Function	Insecticide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea
2. Chemical Abstracts Service (CAS)	N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide
CAS number	116714-46-6
Molecular formula	$C_{17}H_9ClF_8N_2O_4$
Molecular weight	492.71
Structural formula	
Purity of the active ingredient	99.2% nominal (limits 96.5% - 100.0%)

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

Technical Product—Rimon Technical

Property	Result
Colour and physical state	White solid
Odour	Odourless
Melting range	176.5 - 178.0°C

Property	Result	
Boiling point or range	Not applicable	
Specific gravity	1.56	
Vapour pressure at 25°C	1.6×10^{-5} Pascals	
Henry's law constant at 20°C	***N/A***	
Ultraviolet (UV)—visible spectrum	$\lambda_{max} = 253$	
Solubility in water at 20°C	3.4 ± 1.0 µg/L	
Solubility in organic solvents at 20°C	**Solvent** n-Heptane Xylene 1,2-dichloroethane Methanol Acetone Ethyl acetate n-Octanol	**Solubility (g/L)** 8.39 (mg/L) 1.88 2.85 14.5 198.5 113.0 0.98
n-Octanol–water partition coefficient (K_{ow})	log $K_{ow} = 4.3$	
Dissociation constant (pK_a)	Not investigated due to the low water solubility of the test material	
Stability (temperature, metal)	Photochemical degradation half-life = 2.4 hours. Chemically stable on contact with aluminium, aluminium acetate, iron, iron acetate, zinc and zinc acetate at 54°C for 14 days.	

End-use Product—Rimon 10 EC Novaluron Insecticide

Property	Result
Colour	Salmon pink
Odour	Sweet glycol odour
Physical state	Liquid
Formulation type	Emulsifiable concentrate
Guarantee	10% nominal (limits 9.5% - 10.5%)
Container material and description	One litre, white, COEX (coextruded high density polyethylene with a vinyl ethanol polymer barrier) bottles with screw caps and 6 cm openings.

Property	Result
Density	1.078 g/mL at 20°C
pH of 1% dispersion in water	2.9
Oxidizing or reducing action	The product has reducing properties (reacts with potassium permanganate and water).
Storage stability	The product is stable for 2 years when stored at ambient temperature in commercial packaging.
Explodability	The product does not contain any components with explosive properties.

1.3 Directions for Use

Rimon 10 EC Novaluron Insect Growth Regulator is an insecticide for control of Colorado potato beetle and European corn borer on potato and for control of codling moth and Oriental fruit moth on apple and pear. The application rate varies depending on the insect pest (Table 1.3.1). The product is applied as a foliar treatment by ground application only. The minimum reapplication interval is 10-14 days. On potato, Rimon 10 EC Novaluron Insect Growth Regulator is to be applied no more than two times per crop per year, with a maximum application rate of 1640 mL product/ha/crop/season. On apple and pear, the maximum number of applications is four applications per crop per year, with a maximum of 1.95 L product/ha/crop/season.

Table 1.3.1 Insect Control Claims for Rimon 10EC Novaluron Insect Growth Regulator

Pest/Crop	Application Rate
Colorado potato beetle and European corn borer on potato	410 - 820 mL product/ha (44 - 88 g a/ha)
Codling moth and Oriental fruit moth on apple and pear	93-140 mL product/100 L (10 - 15 g ai/100 L). Do not exceed 3500 L water/ha.

1.4 Mode of Action

Novaluron is classified as a Group 15 Insecticide (Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*). It is an insect growth regulator that inhibits chitin synthesis, affecting moulting. Uptake by the pest is mainly by ingestion, but novaluron also works by contact. Application timing and coverage are important for consistent product performance. This active ingredient does not affect the adult stage after development is completed.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Technical Grade of Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Rimon Technical have been validated and assessed to be specific, precise and accurate for the determinations.

2.2 Method for Formulation Analysis

An analytical method was provided for the determination of the active ingredient in the end use product. The method was shown to be linear, precise and specific. Based on the validation data, the method was assessed to be acceptable for use as an enforcement analytical method.

2.3 Methods for Residue Analysis

Gas chromatography with electrochemical detection (GC-ECD) and high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) methods were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant and animal matrices. Adequate extraction efficiencies were demonstrated using radiolabelled cotton gin trash, animal tissues and milk analyzed with the enforcement method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicology database for the new insecticide, Novaluron (Rimon), was conducted. The database is complete, consisting of the full array of toxicity studies currently required for regulatory purposes. The database consists of acceptable studies as well as studies considered suitable for supplemental purposes only. Due to change of ownership of the toxicology database, the applicant is not able to confirm that some studies were carried out in accordance with Good Laboratory Practices (GLP). Similarly, several studies were conducted with batches of chemical of unknown purity. However, there is sufficient information available to conduct a risk assessment.

Novaluron belongs to a novel class of insecticides (benzoylphenol urea compounds) which act by inhibiting chitin biosynthesis in larvae. The main toxicological effect noted in the animal database was oxidative stress and destruction of red blood cells (RBCs), most likely due to the action of an aniline metabolite (3-chloro-4-(1,1,2-trifluoromethoxy) aniline). As a result of erythrocyte destruction, secondary effects were observed in associated blood tissues/organs and included pigmentation in Kupffer cells in the liver as well as macrophages in the spleen. At higher doses, the effect on red blood cell parameters was of a sufficient magnitude to result in hemolytic anaemia and provoke a regenerative response as evidenced by an increase in reticulocytes, Howell-Jolly Bodies and/or Heinz bodies, with accompanying hyperplastic

response in the bone marrow and spleen. Since the turnover of RBCs following oxidative insult progresses with applied dose, a clear adverse effect level for this endpoint was not clearly evident. Criteria were required to characterize when the level of RBC turnover constituted an adaptive response and when the RBC loss was considered adverse to the health of the animals.

Several factors were taken into consideration to determine the level at which decrements in red blood cell mass were adverse to the health of the animal. As a general rule, when the decreases in hematocrit, haemoglobin and red blood cells were about 10% or greater and there were signs of a regenerative response (reticulocytosis, bone marrow hyperplasia, increased mean cell volume, and erythrocytic hyperplasia) and secondary signs of hemolysis were evident (macrophage pigmentation of the spleen, Kupffer cell pigmentation of the liver, increased bilirubin, Howell-Jolly Bodies and/or Heinz bodies were increased), the animals were deemed to have hemolytic anaemia. Changes in only one or two red blood cell mass parameters were not deemed adverse. Data from individual animals were also closely examined to determine the incidence and severity of clinical anaemia. An overall weight of evidence approach was used, integrating all of the above factors to determine the adverse effect level for each study.

Following a single low or repeated low oral dosing regimen, absorption and excretion of Novaluron was low and rapid. The chemical was poorly soluble in water (3µg/L), however, the vehicle used in the metabolism studies. As a result, these results may underestimate the potential bioavailability of the chemical if dissolved in a more appropriate solvent. Whole body and time-course plasma studies revealed that distribution of administered radioactivity is rapid and extensive, with the highest tissue concentration noted in fat, kidney, liver, pancreas, lymph nodes, and adrenals. At 7 days post-dosing, the highest tissue residues were noted in fat, adrenals, epididymis, ovaries, liver, and lymph nodes. Following repeated dosing, concentrations in these tissues were increased by a factor of 3-5, indicating a potential for accumulation of the compound in selected tissues. Peak plasma time was 2-8 hours, regardless of sex, radiolabel or dosage. Excretion occurred primarily by the faecal route (76-95.3%) with minor amounts excreted in the urine (0.6-19.9%), and bile (<1%). No excretion via respiration was detected. The saturation that occurred at the high dose resulted in greater faecal and lower urine/carcass distribution. There were no absorption/excretion differences attributed to gender. Very little metabolism of the parent was noted, with recovery of unchanged parent generally greater than 73%. Metabolites noted in urine were 2,6-difluorobenzoic acid and 3-chloro-4-(1,1,2-trifluoromethoxy) aniline.

Novaluron was of low acute toxicity by the oral, dermal and inhalation routes of exposure, was non-irritating to the skin, minimally irritating to the eyes and was not considered to be a skin sensitizer. The formulated product, Rimon 7.5WDG, containing 7.3 % technical, was considered to be of low toxicity via the oral and dermal routes of exposure, was minimally irritating to the skin, corrosive to the eyes, and was not a skin sensitizer. An inhalation study waiver was accepted for the formulation, since the product is composed of particles too large to be readily inhaled. The formulated product Rimon 10EC, containing 9.3% technical, was considered to be of low toxicity via the oral and dermal routes. A waiver request for the acute inhalation was denied, since the formulated product demonstrated acute effects not noted with the technical grade product. Rimon 10EC was considered to be moderately irritating to eyes, mildly irritating to skin, and a potential skin sensitizer.

A short-term dermal toxicity study showed no skin irritation in any of the test groups after repeated applications of Novaluron to the shaved skin of albino rats. At doses of 75 mg/kg bw/day in males and 400 mg/kg bw/day in females, there were increases in Meth-haemoglobin (Meth-Hb) while adrenal cortex vacuolation was noted in high dose males. The study was deemed supplemental since too few animals were tested, and histology examinations were limited and failed to include several organs considered to be targets of toxicity. However, the lowest dose tested in the study did identify increases in meth-haemoglobin, which was considered to be the salient endpoint of concern for the chemical.

Short-term dietary studies indicated that the hematopoietic system was the target organ in mice, rats, and dogs with rats exhibiting anaemic effects in the form of altered haematology. Secondary organ effects consisted of increased spleen weights as well as increased kidney weights accompanied by cellular changes. The NOAEL in mice was 4.2/4.7 mg/kg bw/day based on increased sulphaemoglobin (sulph-Hb) in females, increased incidence of inclusion bodies, and bilirubin in males and females at a LOAEL of 12.8/15.2 mg/kg bw/day in males and females respectively. The NOAEL in rats was 8.3/8.9 mg/kg bw/day in males and females respectively, based on haematology effects, increased spleen weights and haematopoiesis, and cellularity at the LOAEL of 818.5/871.0 mg/kg bw/day in males and females, respectively. A NOAEL of 10 mg/kg bw/day was noted in dogs, based on haematology changes, increased spleen weights, along with engorged sinusoids, and red pulp congestion of the spleen at the LOAEL of 100 mg/kg/day.

Long term studies in both rats and mice provided no evidence of treatment-induced oncogenicity at any dose level tested. In mice, the NOAEL for chronic toxicity was 3.6/4.3 mg/kg bw/day in males and females, respectively based on hemolytic anaemia, with secondary evidence of oxidative insult and regenerative response including swollen and congested spleens with extramedullary erythropoiesis and hemosiderosis , increased liver weight and decreased adrenal weight (in females) occurring at the LOAEL of 53.4/63.3 mg/kg bw/day in males and females, respectively and above. The NOAEL for chronic toxicity in rats was 30.6/1.4 mg/kg bw/day (in males and females respectively) based on hemolytic anaemia, with secondary evidence of oxidative insult and regenerative response including increased spleen and liver weights, and liver congestion observed at the LOAEL of 884.2/39.5 mg/kg bw/day (in males and females respectively). There appeared to be no durational effects on toxicity noted in the database. Adverse haemolysis was noted at 90 days in subchronic and chronic dosing studies. These effects did not progress in magnitude or severity with prolonged dosing. The NOAEL for carcinogenicity was set at the highest dose tested in both mice (913 mg/kg bw/day) and rats (1113.5 mg/kg bw/day).

Novaluron did not cause point mutations, chromosome aberrations (*in vitro* or *in vivo*), and was not associated with unscheduled DNA synthesis *in vitro*. One exception was the Bacteria DNA Repair assay, for which findings were considered to be equivocal. Overall, there was no evidence to suggest that Novaluron was genotoxic.

Rat and rabbit developmental toxicity studies indicated that Novaluron was not teratogenic. Although an increased incidence of incompletely ossified 5th sternebrae was observed in the

rabbit study, this was not considered to be an adverse event. In both test species, the maternal and developmental NOAELs were set at 1000 mg/kg bw/day, the highest dose levels tested.

In the 2-generation rat reproductive toxicity study, the NOAEL for maternal toxicity was less than 74.2 mg/kg bw/day, the lowest dose level, on the basis of increased body weight gain, and increased spleen weights recorded for females at that dose level. The NOAEL for developmental toxicity was also less than 74.2 mg/kg bw/day on the basis of decreased lactational body weight gain, and increased spleen and liver weight in both F_1 and F_2 pups observed at this dose level. When adult and offspring spleen weights were compared, adults appeared to be more sensitive to the effects of treatment. However, the offspring would have received the treatment (via milk and a small portion in diet during the latter portion of the lactation phase) for 21 days only, compared to the parental treatment duration of 17 weeks. The NOAEL for reproductive toxicity was set at 74.2 mg/kg bw/day on the basis of decreased epididymal sperm count and delayed sexual maturation in the F1 males at 297.5 mg/kg bw/day. Overall, Novaluron was not considered to cause selective toxicity to the developing young.

Novaluron was not neurotoxic (up to limit doses in acute and sub-chronic studies) and there were no indications of endocrine or immune function disruption in the database at doses up to 1820 or 1114 mg/kg bw/day following sub-chronic or chronic dosing respectively.

3.2 Determination of Acceptable Daily Intake

The chronic (lifetime) dietary reference dose is based on the NOAEL of 4.2 mg/kg bw/day from a 90-day feeding study in mice. At the LOAEL of 12.8/15.2 mg/kg bw/day (in males and females respectively), effects included increases in inclusion bodies, bilirubin and sulph-Hb, with associated decreases in RBC parameters. The effect noted in RBCs is considered the salient end point in the database. There did not appear to be a durational effect noted for this endpoint, with the severity of blood turnover not progressing in severity with prolonged dosing. As a result, the NOAEL identified in the 90-day mouse study is considered to be protective for chronic exposure to the chemical. Standard uncertainty factors of 10X for intraspecies variability and 10X for interspecies extrapolation are applied to this NOAEL. This results in an ADI of 0.042 mg/kg bw/day.

The Acceptable Daily Intake is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{UF}} = \frac{4.2 \text{ mg/kg bw/d}}{100} = 0.042 \text{ mg/kg/day of Novaluron.}$$

3.3 Determination of Acute Reference Dose

An ARfD is not required for this product. There were no indications of toxicity following acute exposure, via the oral, dermal or inhalation routes. There were no indications of toxicity noted in the acute neurotoxicity study, nor were there indications of toxicity noted in the developmental toxicity or repeat dosing studies which were considered to have been attributed to a single dose.

3.4 Occupational and Bystander Risk Assessment

3.4.1 Toxicological Endpoints

The formulated product, Rimon 7.5WDG, containing 7.3 % Novaluron, was severely irritating to the eyes, while Rimon 10EC, containing 9.3% technical, was moderately irritating to eyes, mildly irritating to skin, and was considered to be a potential skin sensitizer. A waiver request for the acute inhalation was denied, since the formulated product demonstrated acute effects not noted in the technical grade product.

Toxicological endpoints were derived for occupational exposure following acute, short-term and intermediate-term durations. The predominant route of exposure to Rimon 10EC for handlers and reentry workers is dermal. A 28-day dermal toxicity study was available and was considered to be adequate for endpoint selection for the risk assessment.

There is potential for short-term handler exposure for farmers who spend one to two days mixing, loading and applying the product. There are no acute end points of concern for this product, and as such there is no need for an acute worker exposure risk assessment.

There is potential for acute post-application exposure for consumers who reenter treated orchards in “Pick-Your-Own” operations for hand-harvesting. For the same reasons as mentioned above there is no need for an acute exposure risk assessment.

There is potential for short-term to intermediate-term exposure for workers reentering the treated orchards to perform activities such as hand-thinning, pruning, propping, training, scouting, mowing and hand-harvesting over the full duration of the growing season (from 90-120 days). For short-to-intermediate term exposures, (a few days to several months in duration) a 28-day dermal toxicity study conducted in the rat was considered an appropriate study to protect all populations. At the LOAEL of 75 mg/kg bw/day effects included increases in meth-Hb and decreased body weight gain in males. There was no NOAEL identified for this study as the effects noted above occurred at the lowest dose tested. The effect noted in RBCs is considered the salient end point in the database. There did not appear to be a durational effect noted for this endpoint, with the severity of blood turn-over not progressing in severity with prolonged dosing. As a result, protecting against the effects noted at the LOAEL identified in this study is considered to be protective for short to intermediate exposure to the chemical. Standard uncertainty factors of 10X for intraspecies variability and 10X for interspecies extrapolation are applied to this LOAEL. An additional 3-fold factor was applied for the use of a LOAEL, resulting in a target MOE of 300.

3.4.2 Dermal Absorption

An *in vivo* dermal absorption study was conducted with an end-use formulation containing novaluron (PMRA 1306926). The test substance was applied dermally to groups of four male rats at doses of 1.0, 0.067, 0.0048 or 0.0003 mg/cm^2. Groups of rats were sacrificed 1,2,6,10, 24 or 72 hr after application. Skin washes were performed immediately after sacrifice (or at 24 hr in groups subsequently sacrificed at 72 hr.) Excreta/cage wash were collected at time of sacrifice or

at 24 hr intervals. Skin wash, site covering materials, blood and selected tissues were collected at termination. Tape stripping of the application site was conducted on either 24 hr or 72 hr groups to determine the fate of skin bound residues. Total recovery of radioactivity (mass balance) was acceptable for all dose groups (90.19 - 105.26%). The maximum total absorbed dose, as percentage of administered dose, occurred in the lowest dose group , sacrificed at 72 hr. Total absorbed dose, for this group, was 10.09% (i.e., sum of blood, carcass, fat, untreated skin, total excreted in urine including cage wash and faeces). The amount recovered at the skin test site in this group was 13.91%. As the study duration (3 days) was not long enough to characterize the fate of skin-bound residues, these residues were included in the estimate of absorption. The dermal absorption value, as percentage of administered dose, was determined to be 24%. This estimate is considered conservative as some of the skin bound residues (17%) were removed by tape stripping and these residues are less likely to become absorbed.

As noted above, a 28-day dermal toxicity study was considered appropriate for the occupational risk assessment and the dermal absorption study was not used in the risk assessment. It is noteworthy that poor oral absorption was noted in the oral metabolism study in rats and this would have needed to be taken into consideration if the occupational risk assessment had been based on an oral toxicology endpoint.

3.4.3 Mixer, Loader and Applicator Exposure and Risk Assessment

Exposure estimates were derived for farmers applying Rimon 10EC to potatoes using groundboom equipment and to pome fruit using airblast equipment. For potatoes, the application rate is 44 to 88 gm ai/ha and for pome fruit the application rate is 100-525 gm ai/ha.

Exposure estimates were based on data from the Pesticide Handlers Exposure Database (PHED) Version 1.1, a compilation of generic mixer/loader and applicator passive dosimetry data.

For handler exposure estimates, daily unit exposures from dermal and inhalation routes, normalized to µg ai/kg ai handled, were derived using M/L subsets (liquid; open pour; single layer with gloves) and APPL subsets (groundboom or airblast; open cab single layer); all were high confidence PHED runs with adequate numbers of replicates and A and B grade data. Exposure estimates are presented on the basis of the best-fit measure of central tendency, i.e., summing the measure of central tendency for each body part which is most appropriate to the distribution of data for that body part.

Table 3.4.3.1 Mixer/Loader/Applicator Exposure Estimates for Potato

PHED subset	kg ai handled /day[1]	Dermal Deposition (µg/kg bw/day)		Inhalation (µg/kg bw/day)		Total Exposure[2] (µg/kg bw/day)		MOE[3]	MOE[3]
		farmer	custom	farmer	custom	farmer	custom	farmer	custom
open M/L; open cab: single layer, with gloves for M/L	7.04 farmer 26.4 custom	8.46	31.73	0.26	0.97	8.72	32.7	8600	2300

1 kg ai handled per day = ha treated per day (80 ha for farmer; 300 ha for custom applicator) × application rate (0.088 kg ai/ha)

2 Total exposure is sum of dermal deposition plus inhalation exposure

3 Based on dermal LOAEL of 75 mg/kg bw/day. Target MOE is 300

These margins of exposure exceed the target margin of exposure for both farmers and custom applicators and are considered acceptable.

Mixer/loader/applicator Exposure and Risk Assessment - pome fruit

PHED subset	kg ai handled /day[1]	Dermal Deposition (µg/kg bw/day)	Inhalation (µg/kg bw/day)	Total Exposure[2] (µg/kg bw/day)	MOE[3]
open M/L; open cab: airblast single layer, with gloves for M/L	8.4	105.52	0.82	106.34	705

1 kg ai handled per day = ha treated per day (16 ha for custom applicator) × application rate (0.525 kg ai/ha)

2 Total exposure is sum of dermal deposition plus inhalation exposure

3 Based on dermal LOAEL of 75 mg/kg bw/day. Target MOE is 300

This margin of exposure exceeds the target margin of exposure and is considered acceptable.

3.4.4 Bystander Exposure and Risk Assessment

There is potential for occasional acute exposures to adults and youth during harvesting at commercial pick-your-own farming operations. However, as an acute toxicology endpoint was not identified an acute aggregate exposure and risk assessment is not required.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible.

3.4.5 Exposure and Risk Assessment for Workers Entering Treated Crops

Postapplication exposure estimates were derived for workers who enter treated pome fruit orchards routinely throughout the growing season by coupling dislodgeable foliar residue (DFR) data with activity-specific transfer coefficients.

A chemical-specific DFR study was provided (PMRA 1306927). Field trials were conducted at two sites (California, Pennsylvania) to characterize dissipation of novaluron residues from apple tree foliage following three late season foliar applications of Rimon 6.7 WDG. Using airblast equipment, Rimon 6.7 WDG was applied at a target rate of 380 gm ai/ha, with seven day intervals between applications. Leaf punch samples totalling 405 cm^2 surface area were collected before and after each application; on days 1,2 and 3 after the first and second application; and on days 1,2,3,7,10,14,21,28 and 35 after the third application. Collected field samples were analyzed for novaluron residues using gas chromatography. Additional field fortified samples were collected from an untreated plot and used to determine field recovery. DFR values were corrected for incomplete recovery.

After each application novaluron residues accumulated (0.145 $\mu g/cm^2$, 0.260 $\mu g/cm^2$, 0.408 $\mu g/cm^2$ at the California site; 0.507 $\mu g/cm^2$, 0.785 $\mu g/cm^2$, 1.08 $\mu g/cm^2$ at the Pennsylvania site), and did not decline significantly during the sampling period of 35 days at the California site (0.408 $\mu g/cm^2$ on day 0 after the third application and 0.329 $\mu g/cm^2$ on day 35 after the third application). Residues decline was greater at the Pennsylvania site (1.08 $\mu g/cm^2$ on day 0 and 0.629 $\mu g/cm^2$ on day 35 after the third application). The dissipation curve did not linearly correlate with time at the California site with an R^2 value of 0.102. This limits the utility of the data from the California site. At the Pennsylvania site, the R^2 value was 0.730.

Utility of the data was limited due to several study limitations including limited field recovery data and use of solid formulation rather than a liquid formulation. However, as the Pennsylvania growing regions is similar to Canadian growing regions; the crop (apple), application equipment (airblast) and application regime are relevant to Canada, it was considered appropriate to use the overall average of the dislodgeable foliar residue data from the Pennsylvania site to derive a seasonal average postapplication exposure estimate for pome fruit reentry workers. The overall average DFR value from the Pennsylvania site was 0.73 $\mu g/cm^2$.

Seasonal average exposure estimates were determined by coupling the overall average DFR value with an activity-specific transfer coefficient representative of reentry activities in pome fruit crops. As the applicant is a member of the Agricultural Reentry Exposure Task Force

(ARTF), the ARTF transfer coefficient for hand thinning (3,000 cm^2/hr) was used and is considered conservative. An 8 hour work day and 70 kg bw was assumed. The seasonal average postapplication exposure estimate is 0.24 mg/kg bw/day. Based on the LOAEL of 75 mg/kg bw/day, this yields an MOE of 300. The target MOE is achieved and is considered acceptable.

As the transfer coefficients associated with potato cultivation are generally less than those for pome fruit cultivation, exposure and risk to potato reentry workers is also, therefore, considered acceptable.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products and animal commodities is novaluron. The data gathering/enforcement analytical methodology, Gas chromatography with electrochemical detection (GC-ECD) and high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) methods are valid for the quantification of novaluron residues in apple, pear, potato and ruminant livestock matrices (meat, milk, fat, liver and kidney). The residues of novaluron are stable when stored in a freezer at -18°C for 5 months (pear), 12 months (apple, potato) and 3 months (apple juice). Raw agricultural commodities were processed, residues of novaluron did not concentrate with the exception of wet apple pomace. Supervised residue trials conducted throughout the United States, Canada and Europe using end-use products containing novaluron in or on apple, pear and potato are sufficient to support the proposed maximum residue limits.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.0), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following assumptions were made in a refined chronic analysis: median values for apple and pear, limit of quantitation values for potato, and anticipated residues for animal tissues. The refined chronic dietary exposure from all supported novaluron food uses (alone) for the total population are 2.6% (0.001098 mg/kg bw/day) of the acceptable daily intake (ADI). Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to novaluron from food and water is 5.9% (0.002487 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for all infants (< 1 year) at 17.3% (0.007284 mg/kg bw/day) of the ADI. (Table 3.5.3).

3.5.2.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for novaluron consists of exposure from food and drinking water sources only; there are no residential uses.

3.5.4 Proposed Maximum Residue Limits

Table 3.5.1 Proposed Maximum Residue Limits

MRLs (ppm)	Foods
2.0	Pome fruit (crop group 11)*
0.05	Tuberous and corm vegetable (crop group 1C)*
8.0	Milk, fat
7.0	Fat of cattle, sheep, goat, horse
0.5	Milk
0.4	Liver, kidney, meat and meat byproducts (except liver and kidney) of cattle, sheep, goat, horse
0.01	Fat, liver, kidney, meat and meat byproducts (except liver and kidney) of hog

(* Crop groups are identified in Appendix III).

For additional information on Maximum Residue Limits (MRL) in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and chronic dietary risk estimates are summarized in Tables 3.5.2 and Table 3.5.3 in Appendix I.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Novaluron is expected to enter the terrestrial environment from the application of Rimon 10 EC. Under Canadian field conditions, novaluron is non-persistent to moderately persistent in soils with DT_{50}'s of 18 to 81 days. In water-logged or anaerobic soils, novaluron is moderately persistent with first-order half-lives of 37 to 55 days. Phototransformation of novaluron on soil surfaces is not an important route of transformation in the environment. Novaluron dissipates primarily due to microbial biotransformation. Laboratory and field data indicate that neither novaluron nor its major transformation products are likely to leach into groundwater.

Novaluron may enter the aquatic environment through direct overspray, spray drift, and from surface runoff via sorption to soil particles. The solubility of novaluron is 3.4 µg/L , which makes it practically insoluble in water. The Henry's law constant predicts novaluron to be volatile from a water surface. In aquatic systems, however, novaluron is, expected to dissipate into the sediment, based on its insolubility in water and strong adsorption onto soil/sediment particles. Chemical transformation is not expected to occur in water based on its stability to hydrolysis in acid and neutral sterile surface waters, and stability in sterile soils under sunlight. Considering these properties, novaluron residues are not expected in the air, and very little expected in the water phase. Rapid transformation is expected to occur in aerobic/anaerobic soil and aerobic water/sediment systems. Novaluron is non to slightly persistent in aerobic aquatic water/sediment systems with half-lives ranging from 6.3 to 26 days.

The transformation pathway for novaluron is summarized in Figure 4.1, Appendix I. The major novaluron transformation product, 275-352I, is formed consistently under a wide variety of conditions in terrestrial soils and aquatic water/sediments. Its half life ranges from 25 to 54 days in well aerated soils. In laboratory studies with anaerobic soils, 275-309I and 275-158I are major novaluron transformation products formed in addition to 275-352I. 275-352I, once formed, tends to remain in the sediment or soil. 275-309I in particular, although a minor transformation product in aerobic soil studies, increases with time under both aerobic and anaerobic conditions, and therefore, has the potential to accumulate and persist. While this was a concern in laboratory studies, such persistence was not observed in field studies. 275-158I accumulates and persists under anaerobic conditions only. Under aerobic conditions, 275-158I is rapidly mineralized to CO_2.

A log K_{ow} of 4.3 indicates the potential for novaluron bioaccumulation, which is supported by two bioconcentration studies. In these studies, novaluron was readily accumulated by fish during exposure. Novaluron steady state concentrations were attained within 21-35 days, with bio-concentration factors of 14220-14645x for the whole body. The clearance pattern from the whole body was first-order with half-lives of 11-14 days. Approximately 40 days were required for 95% novaluron depuration from the whole body. The relatively high level of novaluron bioconcentration by fish, its resistance to significant transformation and its slow rate of loss during depuration suggest that it may have some potential for persistence in the aquatic food chain, particularly when frequent applications are made.

Data on the fate and behaviour of novaluron and its major transformation products are summarized in Table 4.1, Appendix I.

4.2 Effects on Non-Target Species

To estimate risk of potential adverse effects on non-target species, a quotient method was used. The risk quotient is calculated by dividing the exposure estimate by a value representing the most sensitive toxic endpoint. Risk quotients (RQs) are initially calculated for a screening-level assessment in order to obtain higher estimates of risk. The screening-level assessment is a realistic worst case scenario and is not beyond the bounds of possibility. "Worst case" involves the application of the active at the highest recommended label rate; in this case, on apples/pears. Low risk is predicted if the risk quotient is less than the trigger value of one. If the trigger values

are exceeded under the screening-level assessment, then a refinement of the assessment is necessary to evaluate how frequently impacts might be expected in the range of conditions that occur in the field. A refined assessment takes into consideration of more realistic exposure scenarios (e.g., solubility considerations, drift to non-target habitats and runoff to water bodies, crops) and may consider different toxicity endpoints.

4.2.1 Effects on Terrestrial Organisms

Screening Level Risk Assessment

Risk of novaluron technical (and/or Rimon 10 EC) to terrestrial organisms was based upon the evaluation of toxicity data for two small mammals (acute oral, dietary, reproduction) and two bird species (acute gavage, short-and long-term dietary exposure, reproduction) representing vertebrates; honeybees (acute contact, acute oral, and a hive/brood study), several predator and parasitoids (one field study), and one earthworm species representing invertebrates; and ten crop species representing plants (Table 4.2, Appendix I). As novaluron is not expected to transform to any great extent on plant foliage and on soil surfaces, the toxicity and risk of 275-352I was not assessed.

For terrestrial vertebrates, novaluron technical was non-toxic to birds and small mammals on an acute oral and acute dietary basis (Table 4.2, Appendix I). There were negligible risks of mortality to these organisms under worst-case scenarios (Table 4.3, Appendix I). Novaluron, however, did cause adverse effects on bird reproduction, including reduced egg laying and duckling/chick survival, with reproductive NOECs of between 30 and 300 mg a.i./kg diet, based on 22-week reproductive studies on mallard ducks and bobwhite quails. Adverse blood and reproductive effects were also observed on rats and mice following a 90-day dietary study. Risk quotients calculated under a conservative worst-case scenario, assuming maximum label application rates, indicate that applications of Rimon 10 EC presents no risks of mortality to birds or small mammals following short-term dietary exposures; risk quotients are less than one (Table 4.3, Appendix I). There are, however, moderate to high risks of reproductive and blood effects, respectively, to birds and rats/mice from continuous long-term dietary exposures, especially at the apple/pear rate, assuming the same conditions as the above; risk quotients range from 1.2 to 10.5. The risk to these organisms under more realistic exposure scenarios is discussed below (see Refined Risk Assessment).

For terrestrial invertebrates, novaluron technical was not acutely toxic (Table 4.2, Appendix I), and neglible acute risks were observed; risk quotients are less than 1 under worst-case scenarios (Table 4.3, Appendix I). Reduced honeybee brood development and colony strength was observed in a hive/brood study at a single application rate of 225 g a.i./ha. In a field study, resident populations of both *Lysiphebus* parasitoid wasps and *Amblyseius* predatory mite nymphs were depressed (approx. 87% reduction compared to controls) for two months following applications of Rimon 10 EC at a rate of 2 × 225 g a.i./ha (7 day interval). Further suppression and reductions, respectively, of non-target beneficials and honeybee brood/colonies cannot be ruled out given the higher application rate of novaluron at the proposed apple/pear rate (4 × 525 g a.i./ha).

A refinement of the exposure scenario for beneficial arthropods could not be made as the screening concentration already considered probable conditions in the field (drift on organisms). In order to mitigate risk, specific instructions to reduce spray drift are provided on the product label to minimize exposure of these organisms.

For terrestrial plants, seedling emergence, phytotoxicity, and vegetative vigour were examined. In pre-emergence applications, no phytotoxicity or effects on plant emergence, crop vigour or plant dry weight were observed. Crop height differences were apparent for soybean, perennial ryegrass and carrots 17-21 days after emergence, however, these differences were less than 25% between the untreated and treated plants. In post-emergence applications, slight crop damage, characterized as chlorosis, and crop vigour differences were noted for sunflower up to 13 days after treatment. Both of these symptoms, however, were transient and not apparent at the later assessment timings. Crop height differences were apparent for onions 14 days after application; these differences were also less than 25% between the untreated and treated plants. No differences in dry weights were apparent at the end of the study. The toxicity to terrestrial plants at the proposed application rates could not be fully assessed based on the submitted data. An application rate of 15 g a.i./ha was used in the submitted study and was considerably less than label application rates of 2 x 88 g a.i./ha for potato and 4 x 525 g a.i./ha for apple/pear orchard use. Because some toxic effects were observed at the 15 g a.i./ha rate (although at less than 25% effect, and with recovery), there is concern that plant toxicity may result at higher application rates. As concerns of drift to non-target terrestrial plants remain unquantified, a buffer zone was caluculated based on the 15 g a.i./ha rate used in the submitted study (Table 4.3, Appendix I). If a new use pattern or application method is requested, a new Tier 1 study with the end use products at application rates equivalent to proposed use rates will be required to quantify the effects on non-target terrestrial plants.

Refined Risk Assessment

During the initial screening level assessment for birds and small mammals, risk was conservatively assessed based on consumption of 100% contaminated diet at a cumulative application rate, assuming no dissipation of product from foliage/food items between applications. If risk was low to negligible with this scenario no further assessment was conducted. If a risk was indicated with this scenario, a more realistic scenario was considered using a single application rate, which assumes the product dissipates from foliage/food items between applications rather than accumulating after each application; this is more realistic as it is expected dissipation will occur between applications through many processes, including wash-off, new plant growth, and transformation. Additionally, although no foliar half-life is available, novaluron dissipation may occur based on the environmental fate information and the food residue data. This scenario is still conservative as it is based on consumption of 100% contaminated diet, and residue levels estimated immediately following a single application. For both the cumulative and single application rates, when a risk exists based on consumption of 100% contaminated diet, a determination was made of the percentage of diet required to be contaminated in order to result in a risk quotient of 1.0 (moderate risk), and the likelihood that this percentage of contaminated diet would be consumed by the animal. Additionally, other factors were considered when assessing the risk, including the toxic effects observed in the laboratory studies, properties of the chemical, and the use pattern.

The risk of reproductive effects from use of novaluron at apple/pear rates to both bobwhite and mallard was further considered. Based on a conservative estimation of exposure using the cumulative application rate, 82% of the bobwhite quail diet and 42% of the mallard diet would need to be contaminated to reach a risk quotient of 1 (risk exists). It is unlikely this high percentage of contaminated diet would be consumed continuously over an extended time period, particularly for the bobwhite quail. The reproductive risk was also assessed using an EEC based on a single application; this represents a more realistic scenario (see above). Using a single application for the orchard use, the risk of reproductive effects in both bobwhite quail (RQ = 0.306) and mallard (RQ = 0.6) was considered low. Therefore, based on more realistic scenarios, the reproductive risk to mallard and bobwhite is expected to be low.

It is noted that the dietary toxicity endpoint for rat and mouse is based on a 90-day study with *continuous* exposure, and the toxicity effects observed were blood effects; no mortality or body weight effects were noted. Additionally, the screening level risk assessment was based on the dietary concentration where no adverse effects were observed (NOAEC), while the lowest concentration where adverse effects were observed (LOAEC) was several magnitudes higher than the NOAEC, particularly in the case of rats. Risk quotients based on the NOAEC range between 0.89 to 35.1 for both rats and mice. Corresponding risk quotients based on the LOAEC range between 0.0089 and 10.5. It is possible that a rat or mouse living within an orchard may consume contaminated dietary items in quantities sufficient to experience toxic effects on blood, however, mortality is not expected from dietary consumption and the populations of mice or rats near an orchard are not likely to be impacted by dietary exposure to this chemical. Therefore, the dietary exposure of mice or rats in orchards was not considered to be a significant concern.

On apple/pear orchards, reproductive risk to small mammals was estimated to be moderate based on a cumulative application rate (RQ = 1.0). In this scenario, 100% of the diet would need to be contaminated with novaluron to reach a risk quotient of 1 (moderate risk). Similarly to the refined assessment for birds, it is very unlikely to have consumption of 100% contaminated diet for small mammals. Because the toxicity endpoint used in the screening level assessment is a LOAEC rather than a NOAEC, the risk was further assessed. Based on a more realistic scenario, using an expected environmental concentration calculated from a single application rate, no further reproductive risk was found (RQ = 0.26). In this scenario, 385% of the diet consumed would need to be contaminated in order for the existence of a risk (i.e. nearly four times more food than is consumed). It is unlikely a reproductive risk would exist to small mammals, even considering that the toxicity endpoint is a LOAEC. For the proposed orchard use of this product, no further reproductive risk is expected.

On potato, reproductive risk was estimated to be negligible based on a cumulative application rate (RQ = 0.089) and based on a single application rate (RQ = 0.044). In these scenarios, consumption of over 100 times more food than is normally consumed, and all of it contaminated, would be required in order for a risk to occur. This indicates that it is extremely unlikely a reproductive risk would be posed to small mammals, even considering that the toxicity endpoint is a LOAEC. For the proposed potato use of this product, the reproductive risk to small mammals is expected to be negligible.

Terrestrial Risk Mitigation Measures
The terrestrial risk assessment of novaluron identified areas of concern, particularly with non-target terrestrial arthropods (ie. honeybees, predatory mites, parasitoid wasps), and non-target terrestrial plants. As there is concern of drift to non-target terrestrial plants a terrestrial buffer zone of 1-30 m, depending on the crop and application method, was calculated based on the conservative end-point of 15 g a.i./ha rate used in the submitted study (Table 4.2, Appendix I). Risks to non-target terrestrial arthropods, will be mitigated by the use of environmental hazard statements on the label.

4.2.2 Effects on Aquatic Organisms

Screening Level Risk Assessment
Risk of novaluron technical to aquatic organisms was based upon the evaluation of toxicity data for five freshwater species (one invertebrate, one algae, one vascular plant, and two fish); and three estuarine/marine species (one crustacean, one mollusk, and one fish) following worst-case scenario exposures (Table 4.2, Appendix I). Results from an outdoor microcosm community study, where effects on freshwater aquatic invertebrates were assessed, were also used. The risk assessment of 275-352I on aquatic organisms was based on only three studies; one of each on a freshwater aquatic invertebrate, fish, and algae. Likewise, the risk assessment of Rimon 10 EC was based on a freshwater fish, invertebrate, and vascular plant.

In acute dose-response and long-term studies, novaluron did not cause any mortality or sublethal effects to fish, nor was any toxicity observed on green algae up to the limit of solubility (3.4 µg/L). Rimon 10 EC and the transformation product 275-352I, however, were slightly toxic and moderately toxic, respectively, to fish. The toxicity of novaluron to amphibians was estimated using endpoints from acute and 28-day exposure fish studies as surrogate data. Risk quotients calculated under a conservative worst-case scenario, assuming maximum label application rates, indicate that novaluron and Rimon 10 EC present no risks of mortality to fish, vascular plants, amphibians and algae following short- or long-term exposure; risk quotients are less than one (Table 4.3, Appendix I). There is, however, some risk of behavioural effects (hyperventilation, coughing, lethargy, loss of coordination) to rainbow trout, and amphibians with risk quotients of 0.47 to 75 (Table 4.3, Appendix I), depending on the crop, resulting from prolonged exposure to the conservative direct overspray application of novaluron and Rimon 10 EC. There is also some risk to fish from exposure to 275-352I at the apple/pear application rate, with the risk quotient being >2.4. No risk was found at the potato rate; the risk quotient was less than one.

In laboratory studies, novaluron, Rimon 10 EC, and the transformation product, 275-352I, were moderately toxic to very highly toxic to aquatic invertebrates (pelagic and benthic) and mollusks. The susceptibility of aquatic invertebrates to novaluron was confirmed in an outdoor microcosm study. On a chronic basis, novaluron negatively affected growth and reproduction of mysid shrimps at concentrations as low as 26.1 ng a.i./L. Exposure of freshwater and estuarine aquatic invertebrates to Rimon 10 EC exhibited the same mortality response. The risk quotients to novaluron, Rimon 10 EC, and 275-352I, calculated under the realistic worst-case scenarios, greatly exceed the trigger value of one by three to four orders of magnitude. The most sensitive freshwater and marine organisms were daphnia magna and mysid shrimps, both aquatic invertebrates. In general, aquatic invertebrates (pelagic and benthic) and mollusks appear to be at

extremely high risk, resulting from acute and/or chronic exposures to novaluron, than their vertebrate counterparts. Considering that novaluron is a chitin synthesis inhibitor, such effects and risks to aquatic invertebrates were expected.

Refined Risk Assessment

Novaluron Technical: The identified risks to aquatic organisms, mentioned previously, were based on a worst-case scenario, involving exposure via a direct-spray with the cumulative application rate; 490 µg a.i./L and 52 µg a.i./L for apples/pears and potato applications, respectively. The direct-spray assumes that 100% of the applied material drifts into the aquatic or terrestrial environment and is available for biological uptake, regardless of its physico-chemical properties (e.g., solubility, adsorption), and most probable source (eg. drift, runoff, groundwater, etc.). A refined assessment considered that the most likely routes of entry of novaluron into water are through drift (Table 4.4, Appendix I). For drift, the screening level assumes 100% drift to a water body. The actual maximum drift deposition on bare ground expected at one metre downwind from the point of application is 74% (early airblast) and 6% (ground), respectively, for apple/pear and potatoes. Using the corresponding expected concentration of novaluron in water still led to risk quotients higher than one for all organisms identified as being at risk under a worst-case scenario (Table 4.4, Appendix I). Further refinement in the assessment involved the determination of risk at the novaluron solubility limit (3.4 µg/L), as free-swimming aquatic organisms are not expected to be exposed to concentrations beyond this value. Even at novaluron concentrations as low as the solubility limit (3.4 µg/L), however, aquatic invertebrates, mollusks, and microcosm communities continue to be at risk from acute and/or chronic exposures with risk quotients greater than one by one to two orders of magnitude (Table 4.4, Appendix I).

Following the risks of novaluron toxicity to aquatic invertebrates and mollusks at the solubility limit, a refined assessment was conducted. Accordingly, the most likely routes of novaluron entry into water are primarily through drift and surface water runoff. Therefore, risks to these above organisms were determined at expected environmental concentrations based on a runoff simulation model, with 10% drift taken into account, for apple/pear and potato applications. The simulated water body consisted of a 1 ha wetland with an average depth of 80 cm and a 10 ha drainage area. From the simulation, peak concentrations for apple/pear and potato applications in runoff water were 1.64 and 0.77 µg a.i./L, respectively [6]. Corresponding peak sediment interstitial water concentrations were 113 and 77 ng a.i./L[7]. At these expected concentrations, free-swimming aquatic invertebrates, such as daphnia, remain at risk to novaluron, resulting from acute and chronic exposures, at both apple/pear and potato application rates; risk quotients

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[6] For the 4 × 525 g a.i./ha apple/pear application, peak, 96 hour, 21 day, 60 day, 90 day, and yearly conservative EECs were 1.64, 0.69, 0.25, 0.14, 0.15, and 0.075 µg a.i./L, respectively. Corresponding conservative EECs for the 2 × 88 g a.i./ha potato application were 0.77, 0.35, 0.16, 0.99, 0.084, and 0.041 µg a.i./L, assuming that 10% of spray drift entered the simulated waterbody.

[7] For the 4 × 525g a.i./ha apple/pear application, peak, 96 hour, 21 day, 60 day, 90 day and yearly conservative sediment interstitial pore water EECs were 113, 113, 110, 105, 101 and 60 ng a.i./L, respectively. Corresponding conservative sediment interstitial pore water EECs for the 2 x 88 g a.i./ha potato application were 77, 77, 74, 65, 62 and 37 ng a.i./L, assuming that 10% of the spray drift entered the simulated waterbody.

range from 3.8 to 8.4 (Table 4.4, Appendix I). Based on both free-water and sediment interstitial pore-water concentration simulations, risks also remain for significant impacts to microcosm communities, including both free-swimming and sediment-dwelling aquatic invertebrates (pelagic and benthic), resulting immediately after a simulated application (peak) and after longer term exposures (>90 days) for apple/pear and potato uses; risk quotients range from 1.3 to 33 (Table 4.4, Appendix I). There is risk to marine mollusks, after 21 days of exposure simulation, only when novaluron is applied on potatoes. In general, aquatic invertebrates that live in or on freshwater lake, river, or estuarine sediments are particularly susceptible and at risk considering that all aspects of their life cycles are spent in direct contact with sediment and associated interstitial water for an indefinite period of time, and that novaluron rapidly dissipates from the water phase to the sediment phase (Figure 4.1, Appendix I).

The risk of behavioural effects to rainbow trout and amphibians at the novaluron solubility limit, and at refined assessment concentrations, are negligible. It was not possible to conduct a refined risk assessment of Rimon 10 EC to rainbow trout and amphibians because of the associated formulants. The chronic risk to amphibians was assessed using a surrogate prolonged 28-day rainbow trout study because of deficiencies relating to the detection and quantification of novaluron in the submitted surrogate fish early life-cycle study. Such deficiencies were also the case regarding the risk assessment of novaluron on marine fish. Considering the mode of action of novaluron, however, marine fish and amphibians are not expected to be at risk from exposures to the Rimon 10 EC formulation and novaluron.

275-352I: The risks of susceptible organisms to 275-352I, described above, assumed a 100% conversion of novaluron to the transformation product. A more realistic exposure scenario, however, would involve the assumption of a 22% conversion from novaluron, based on the transformation patterns observed in a submitted aerobic water/sediment fate study. As such, the refined expected environmental concentration of 275-352I would be 0.077 and 0.0081µg/L for the direct application of novaluron at the apple/pear and potato rates, respectively. At these concentrations, the risk to aquatic organisms would generally decline. Risks of mortality, from the refined acute exposures, remained for aquatic invertebrates, however, were no longer apparent for fish and freshwater algae at both apple/pear rate and potato rates.

Aquatic Risk Mitigation Measures

The aquatic risk assessment of novaluron, Rimon 10 EC, and 275-352I identified areas of concern, particularly with aquatic invertebrates (benthic and pelagic) and marine mollusks. Therefore, mitigation measures, by way of buffer zones and environmental hazard statements, are required for the protection of these organisms. The most sensitive endpoint chosen for the buffer zone calculations was the chronic daphnia. This endpoint was chosen because it affords greater protection for freshwater benthic invertebrates (gammarids), which were more sensitive than daphnia in a community microcosm study. In this study, the daphnia fully recovered, however, gammarids were completely eliminated and experienced no recovery whatsoever. Buffer zones to protect aquatic organisms range from 3 to 80 metres, depending on the crop, application method, type of habitat, and stage of growth.

5.0 Value

5.1 Effectiveness Against Pests

Twelve small-plot trials conducted from 1999 to 2004, and 13 small-plot trials conducted from 2000-2003 were evaluated to support proposed label claims for potato and for apple, respectively. All trials were conducted in the United States or Canada. For each trial, an appropriate experimental design was employed, which included an untreated control as well as a positive control.

The control of individual insect species or the reduction in damage caused by insect pests was assessed and compared to an untreated control. Observations were made at various times throughout the growing season after treatment occurred.

No trials were provided on pear for control of codling moth and Oriental fruit moth, and only one trial was provided for European corn borer control on potato. Therefore, data generated on apple were extrapolated to pear and those generated on snap bean and pepper were extrapolated to potato for control of the respective pests. Pest biology and feeding damage are expected to be similar between crops, making extrapolation possible.

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Foliar applications of Rimon 10 EC Novaluron Insect Growth Regulator

Efficacy data established the lowest effective rate for proposed pests, and acceptable application rates are identified in Table 5.1.1.

Table 5.1.1 Use claims for Rimon 10EC Novaluron Insect Growth Regulator

Pest/Crop	Application Rate
Colorado potato beetle and European corn borer on potato	410 - 820 mL product/ha (44 0 88 g a/ha)
Codling moth and Oriental fruit moth on apple and pear	93-140 mL product/100 L (10 - 15 g ai/100 L). Do not exceed 3500 L water/ha.

5.1.1.2 Total Spray Volume

Novaluron acts primarily through ingestion with some contact activity. Therefore, thorough, uniform coverage is essential for optimum control. The minimum recommended spray volume on potato is 100 L/ha, applied by conventional ground application equipment. On apple and pear, a minimum water volume of 700 L/ha applied by conventional ground application equipment is recommended for trellised trees or trees 3 metres tall or less. For trees over 3 metres tall, a minimum water volume of 935 L/ha is recommended. The maximum water volume which can be applied to apples and pears is 3500 L/ha.

5.1.1 Tank-mix Combinations

Tank mixes with Rimon 10 EC Novaluron Insect Growth Regulator were not proposed.

5.2 Phytotoxicity to Host Plants

No phytotoxicity to target plants was reported in any of the trials conducted with novaluron.

5.3 Impact on Succeeding Crops

The impact on succeeding crops was not evaluated in this submission.

5.3.1 Acceptable Claims for Rotational Crops

Rotational crops were not assessed in this submission.

5.4 Economics

No market analysis was assessed for this submission.

5.5 Sustainability

5.5.1 Survey of Alternatives

Alternative active ingredients vary depending on the pest/crop combination, and are listed in Appendix 1 for Colorado potato beetle and European corn borer on potato (Table 5.5.1) and codling moth and Oriental fruit moth on apple and pear (Table 5.5.2). Many of the currently available alternatives for Colorado potato beetle on potato and for control of codling moth on apple and pear are older classes of insecticides, such as carbamates, organophosphates, and chlorinated cyclodienes. Fewer alternative active ingredients are registered for control of European corn borer on potato (see Table 5.5.1) or Oriental fruit moth on apple and pear.

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Rimon 10 EC Novaluron Insect Growth Regulator is compatible with current chemical and cultural management practices and can be applied with conventional ground application equipment. Growers are familiar with the monitoring techniques to determine if and when applications are needed.

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

Novaluron is a benzolyurea insecticide, which is a chitin synthesis inhibitor. Novaluron acts by inhibiting chitin biosynthesis and interfering with cuticle formation in larvae. While novaluron

does not have ovicidal activity, it does lead to mortality of first instars that hatch from eggs laid on sprayed foliage. It has no effect on adults which have completed development.

Development of resistance to novaluron has not been reported. However, a resistance management strategy should be followed, and the label for Rimon 10 EC Novaluron Growth Regulator includes the resistance management statements, as per Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

Cyromazine, another insect growth regulator, is registered for use against Colorado potato beetle in potatoes since 1996. This active ingredient is also a chitin synthesis inhibitor, but is classified as a Group 17 class of insecticide. Although there are no reports of cross-resistance between these two active ingredients in Colorado potato beetle, potential cross resistance between these two classes of insecticides should be monitored.

5.5.4 Contribution to Risk Reduction and Sustainability

Novaluron is a classified as a Group 15 insecticide, which is a new chemistry for control of Colorado potato beetle and European corn borer on potato, and for control of codling moth and Oriental fruit moth on apple and pear.

On potato, new chemistries are needed to help prevent the development of resistance, which has been a problem with Colorado potato beetle. On apple and pear, Rimon 10 EC is an alternative to older insecticides, such as organophosphates, used for control of major pests.

Novaluron is not acutely toxic to birds, fish, and small wild-mammals while several of the alternative products are extremely toxic to these organisms (azinphos-methyl, endosulfan, rotenone, deltamethrin, permethrin, carbofuran). Novaluron may cause temporary suppression of beneficial arthropods other than bees. However, it is generally not as acute toxic to these organisms compared to other alternatives (spinosad, carbaryl). Buffer zones are required for the protection of both terrestrial and aquatic organisms from novaluron spray drift. Novaluron contains no formulants of concern. On the other hand, novaluron itself is extremely toxic to aquatic invertebrates. Novaluron has very little potential to leach to groundwater compared to imidacloprid, and therefore, has very little potential to contaminate groundwater. Novaluron is slightly persistent in soil and sediments and is not expected to carryover into the following season.

The dietary risk on human health associated with the use of novaluron has been assessed. The findings indicate that there is no unacceptable health risk imposed to the general population including infants, children, adults and seniors resulting from food (including water) consumption as a consequence of the use of novaluron in accordance with the label directions.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's *Toxic Substances Management Policy*, which puts forward a preventive and precautionary approach to deal with

substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

While reviewing Novaluron, the PMRA took into account the federal Toxic Substances Management Policy and followed its Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of Novaluron were also considered, including major transformation products formed in the environment, microcontaminants in the technical active, and formulants in the end-use product, Rimon 10 EC. The PMRA has reached the following conclusions:

- Novaluron does not meet the criteria for persistence. Studies have indicated that its first-order half-life values in air (n/a non-volatile), sediment (8.2-28 days) and soil (DT_{50}: 6.9-55 days) are below the TSMP Track-1 cut-off criteria for air (≥2 days), soil (≥182 days), and sediment (≥365 days). Novaluron is expected to partition rapidly into the sediment, where transformation will occur.

- Novaluron is bioaccumulative. The *n*-octanol–water partition coefficient (log K_{ow}) is 4.3, which is below the TSMP Track-1 cut-off criterion of ≥5.0. However, studies have determined that the bioconcentration factor (BCF) is between 14220x and 14645x that of the concentration in water, which is greater than the TSMP Track-1 cut-off criterion of BCF ≥ 5000.

- Novaluron meets the CEPA definition of toxicity

- Novaluron is anthropogenic.

- No data is available on the persistence of the major transformation products, 275-352I, 275-309I, and 275-158I in soil. However, based on the QSAR method, by Meyland and Howard (1995), log K_{ow}s were estimated to be 3.02, 3.38, and 1.18 for 275-352I, 275-309I and 275-158I, respectively. These transformation products are not expected to be persistent in the environment.

- Novaluron (technical grade) does not contain any by-products or microcontaminants that meet the TSMP Track-1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

- The formulated end-use product is not known to contain any U.S. EPA inert List 1 or 2 formulants or any known TSMP Track-1 substances.

Therefore, the use of Novaluron is not expected to result in the entry of Track 1 substances into the environment.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for novaluron is adequate to define the majority of toxic effects that may result from human exposure to novaluron. Long term studies in both rats and mice provided no evidence of treatment-induced oncogenicity at any dose level tested. There appeared to be no durational effects on toxicity noted in the database. Adverse haemolysis was noted at 90 days in subchronic and chronic dosing studies, and these effects did not progress in magnitude or severity with prolonged dosing. Overall, there was no evidence to suggest that novaluron was genotoxic, teratogenic or neurotoxic.

Acceptable margins of exposure are obtained for mixer/loader/applicators and reentry workers. An aggregate exposure assessment (dietary + residential) was not conducted for novaluron as no acute toxicology endpoint was identified.

The nature of the residue in apple, potato, cabbage, cotton and goat is adequately understood. The residue definition is novaluron. The proposed uses of novaluron on apple, pear and potato do not constitute an unacceptable chronic dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified:

residues of novaluron in and on pome fruit (crop group 11) (2.0 ppm);
tuberous and corm vegetable (crop group 1C) (0.05 ppm);
Milk, fat (8.0 ppm);
Fat of cattle, sheep, goat, horse (7.0 ppm);
Milk (0.5 ppm);
Liver, kidney, meat and meat byproducts (except liver and kidney) of cattle, sheep, goat, horse (0.4 ppm); and
Fat, liver, kidney, meat and meat byproducts (except liver and kidney) of hog (0.01 ppm).

7.2 Environmental Risk

Novaluron, and its metabolite 275-352I, present a low risk to wild mammals, birds, earthworms, fish, algae, and aquatic plants. Non-target terrestrial arthropods (honeybees, predatory mites, parasitoid wasps) and aquatic invertebrates (sediment dwelling and open-water), however, are at risk. Buffer zones are needed to protect the aquatic organisms and terrestrial plants. Buffer zones are required to protect aquatic organisms and non-target plants from novaluron resulting from Rimon 10 EC application spray drift. The buffer zone vary from 3 to 80 metres for aquatic organisms, and 1 to 30 metres for non-target plant species Environmental hazard statements are provided on the product label for the protection of honeybees, beneficial insects, and non-target terrestrial arthropods.

7.3 Value

Efficacy data support the use of Rimon 10 EC Novaluron Insecticide for control of Colorado potato beetle and European corn borer on potato, and control of codling moth and Oriental fruit moth on apple and pear. Applications must be made according to the use instructions identified on the label.

7.4 Unsupported Uses

Certain uses originally proposed by the applicant were not supported by the PMRA because value has not been adequately demonstrated. Unsupported uses are outlined in Table 7.1 (Appendix I).

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing full registration for the sale and use of the technical grade active ingredient Novaluron Insecticide and the end-use product Rimon 10 EC to control Colorado potato beetle and European corn borer on potato and codling moth and Oriental fruit moth on apple and pear by foliar application. An evaluation of current scientific data from the applicant, scientific reports and information from other regulatory agencies has resulted in the determination that, under the proposed conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
bw	body weight
CAS	chemical abstracts service
cm	centimetres
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in the test population)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in the test population)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
ER_{25}	effective rate for 25% of the population
g	gram
ha	hectare(s)
HDT	highest dose tested
Hg	mercury
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable

NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PBI	plantback interval
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RSD	relative standard deviation
SC	soluble concentrate
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 5.5.1 Alternative active ingredients for control of Colorado potato beetle (CPB) and European corn borer (ECB) on potato

Group	Chemical Group	Active Ingredient	Pest
1A	Carbamates	carbaryl	CPB, ECB
		carbofuron, oxymyl	CPB
1B	Organophosphates	azinphos-methyl	CPB, ECB
		chlorpyrifos, diazinon, disulfoton, malathion, methamidophos, naled, phosmet	CPB
2A	Chlorinated cyclodienes	endosulfan	CPB
3	Diphenylethane	methoxychlor	CPB
	Synthetic pyrethroids	cyhalothrin-lamda, cypermethrin, deltamethrin, permethrin	CPB
	Pyrethrins	pyrethrins	CPB
4	Chloronicotines	imidacloprid, acetamiprid	CPB
5	Spinosyns	spinosad	CPB, ECB
11	Bt micobials	*Bacillus thuringiensis*	CPB, ECB
17	Triazine (inhibits chitin biosynthesis)	cyromazine	CPB
21	Botanical	rotenone	CPB, ECB
N/A	not classified	diatomaceous earth (silicon dioxide)	CPB
N/A	not classified	potassium salts of fatty acids	CPB

Table 5.5.2 Alternative active ingredients for control of codling moth (CM) and Oriental fruit moth (OFM) on apple and pear

Group	Chemical Group	Active Ingredients	Crop/Pest
0.042	Carbamates	carbaryl, methomyl	apple and pear/CM
1B	Organophosphates	azinphos-methyl, diazinon, malathion, phosalone, phosmet	apple and pear/CM

Group	Chemical Group	Active Ingredients	Crop/Pest
0.083	Chlorinated cyclodienes	endosulfan	apple and pear/CM
3	Synthetic pyrethroids	cyhalothrin-lamda, cypermethrin, permethrin	apple and pear/CM
		deltamethrin	apple and pear/CM and OFM
4	Chloronicotines	acetamiprid	apple and pear/CM
18	Benzoic acid hyrazide (ecdysone agonist/disruptor)	tebufenozide	apple/CM
			pear/CM (British Columbia only)
		methoxyfenozide	apple/CM and OFM
N/A	not classified	diatomaceous earth (silicon dioxide)	apple and pear/CM and OFM
N/A	not classified	pheromone-based mating disruption	apple and pear/CM and OFM

Table 7.1 Label Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant-proposed Label Claims	Accepted Label Claims	Unsupported Label Claims
Codling moth, Oriental fruit moth, leafminers (spotted tentiform and western tentiform), pear psylla, oblique banded leafroller, plant bug, white apple leafhopper, redbanded leafroller, fruittree leafroller, variegated leafroller, tufted apple budmoth, eyespotted budmoth on apple and pear	Codling moth and Oriental fruit moth on apple and pear	leafminers (spotted tentiform and western tentiform), pear psylla, oblique banded leafroller, plant bug, white apple leafhopper, redbanded leafroller, fruittree leafroller, variegated leafroller, tufted apple budmoth, eyespotted budmoth on apple and pear
Colorado potato beetle, European corn borer, Armyworms, foliage feeding caterpillars, Potato tuber whiteflies on potato	Colorado potato beetle and European corn borer on potato	Armyworms, foliage feeding caterpillars, Potato tuber whiteflies on potato

Table 3 Toxicology Endpoints for Use in Health Risk Assessment for Novaluron

METABOLISM (0.5% carboxymethylcellulose)

Sprague-Dawley rats received by gavage, either a single low oral dose (2 mg/kg), a repeated low oral dose (2 mg/kg for 14 days), a single high oral dose (1000 mg/kg) of [chlorophenyl-^{14}C(U)] "RIMON" or a single low oral dose (2 mg/kg) of [difluorophenyl-^{14}C(U)] "RIMON".
Rate and extent of absorption and excretion: Absorption was low and rapid for both radio-labels, with saturation of absorption noted following high dosing:
[chlorophenyl-^{14}C(U)]: Low Dose(6 - 7%). Repeat Low (10-14%). High Dose (0.7%).
[difluorophenyl-^{14}C(U)]: Low Dose(18.5-20.7%). Peak plasma time was 2-8 hours for both radio-labels.
Excretion was mainly by faecal route (76-95.3%), of which parent was the only major contributor to the overall radioactive content. Faecal excretion was generally complete by 72 hours post-dosing (94-99%). There was no excretion via respiration, while urinary excretion was generally low (0.6-19.9%). Urinary excretion was slow, reflecting tissue sequestration, with only 63-74% complete by 72 hours post-dosing. Biliary excretion was insignificant. (<1%). Carcass contained 0.1 - 3.1% after 48 hours. There were no absorption/excretion differences attributed to gender.
Distribution / target organ(s): Distribution to all body compartments was rapid and extensive, with highest tissue concentrations noted in fat, kidney, liver, pancreas, lymph nodes, ovaries and adrenals. At 7 days post-dosing the highest tissue residues were noted in fat, adrenals, epididymis, ovaries, liver and lymph nodes, at concentrations exceeding peak plasma levels. Following repeated dosing, concentrations in these tissues were increased by a factor of 3-5, indicating a potential for accumulation in fatty tissues. Parent was the only identified source of recovered tissue radio-activity.
Toxicologically significant compound(s): Very little metabolism of the parent was noted, with recovery of unchanged parent generally greater than 73%. Metabolites noted in urine were 2,6-difluorobenzoic acid (10-24%) and 3-chloro-4-(1,1,2-trifluoromethoxy) aniline (<1%).

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
ACUTE STUDIES			
Oral Gavage (93.5% purity)	Sprague Dawley Rats (2/sex) at doses of 0, 500, 1000, 3500, or 5000 mg/kg bw in 0.5% carboxymethylcellulose and Tween 80	LD_{50} > 5000 mg/kg bw (♂/♀)	No mortalities, clinical signs of toxicity or abnormalities noted. **LOW Toxicity**
Dermal (94.3% purity)	Sprague Dawley Rats (5/sex) at limit doses of 2000 mg/kg bw	LD_{50} > 2000 mg/kg bw (♂/♀)	No mortalities, clinical signs of toxicity, dermal irritation or abnormalities noted. **LOW Toxicity**
Inhalation (96.7% purity)	Sprague Dawley Rats (5/sex) 4 hours, head only, at concentrations of 0 or 5.15 mg/L (analytically determined)	LC_{50} Males and Females > 5.15 mg/L	Clinical signs included laboured breathing and unkept appearance during exposure. Clinical signs resolved by 2 hours post-dosing. No mortalities **LOW Toxicity**

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Skin Irritation (94.3% purity)	New Zealand White Rabbits, (1 male, 5 females) 0.5 g applied for 4 hours.	No dermal irritation or signs of toxicity during the course of the observation period. Erythema and Edema scores were 0 for all animals, for all times tested. **non-irritating to the skin**	
Eye Irritation (94.3% purity.)	6 male New Zealand White Rabbits, 0.1 mL instillation	Mild conjunctival inflammation was noted in all animals 1 hour post-dosing; resolved by 24 hours post-treatment. **Minimally irritating to the eyes**	
Dermal Sensitization (96.7% purity)	Dunkin Hartley Guinea pigs (10 males) tested at 10% in DMSO (Buehler) Positive control: none		No dermal reactions. Unacceptable due to lack of GLP, too few animals used, not sufficiently high enough concentrations
Dermal Sensitization (96.7% purity)	Dunkin Hartley Guinea pigs (20 males) tested at 80% and 40% in acetone; (Magnusson-Kligman Maximization) Positive control: HCA	Negative	No dermal reactions during induction or challenge. **Not a skin sensitizer under the conditions of this test**
ACUTE STUDIES - FORMULATION Rimon 7.5 WDG			
Oral	Sprague-Dawley Rats (3 /sex) limit dose: 5000 mg/kg bw	LD_{50}> 5000 mg/kg bw	No mortalities. Clinical signs such as pilo-erection, hunched posture, lethargy, abnormal gait (all treated animals). Five animals recovered fully. All animals except one female gained weight. **Low Toxicity**
Dermal	Sprague-Dawley Rats (5/sex) at limit dose of 5000 mg/kg bw.	LD_{50}> 5000 mg/kg bw	No mortalities. Very slight to slight dermal irritation was noted in 7 animals. **Low Toxicity**
Acute Inhalation	Not conducted: Study waiver request		Waiver accepted on the basis that the granule size of the EUP will not pose an inhalation hazard.
Dermal Irritation	New Zealand White rabbit (3, sex not stated); 0.5 g applied for 4 hours	MAS = 1 MIS = 2	**Minimally irritating**
Eye Irritation	New Zealand White Rabbits (2 male, 1 female); 0.1 mL instillation	MAS=44.3 MIS=48.3	No mortalities. Well-defined irritation. **SEVERE irritant** (more than half of the individual scores at 7 days greater than 10)

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
Dermal Sensitization	Dunkin Hartley Guinea Pig; (Magnussen Kligman method); at 5% and 2% w/w in distilled water Positive Control: 2-mercaptobenzothiazole		Slight to well-defined erythema (intradermal and topical induction). No skin reaction at challenge. **Not a skin sensitizer under the conditions of this test.**
ACUTE STUDIES - FORMULATION RIMON 10 EC			
Oral	Sprague-Dawley Rats (5/sex) at a limit dose of 5000 mg/kg bw.	LD_{50}> 5000 mg/kg bw	No mortalities. Clinical signs of toxicity were pilo-erection, hunched posture, waddling gait, lethargy, decreased respiration rate, bright yellow stained urine. All animals gained weight over the course of the study. **Low Toxicity**.
Dermal	Sprague-Dawley Rats (5/sex) at a limit dose of 2000 mg/kg bw	LD_{50}> 5000 mg/kg bw	No mortalities. No signs of clinical toxicity except for occasional transient and slight dermal irritation. One male and all females had a slight lower body weight gain by Day 8 with a similar trend for one male and two females by Day 15**. Low Toxicity**
Inhalation	Not conducted: Study waiver request		Waiver request denied on the basis that the EUP is demonstrating effects not seen with the Technical.
Eye Irritation	New Zealand White rabbits (2 males, 1 female) 0.1 mL instillation	MAS=25 MIS= 32	**Moderately Irritating**
Dermal Irritation	New Zealand Rabbit (6 males) 0.5mL for a 4 hour exposure.	MAS=2.4 MIS=2.8	**Mildly Irritating**
Dermal Sensitization	Dunkin Hartley Guinea Pig (20 males /test group); (Magnussen Kligman method) at 15% and 30% w/v in water Positive control: HCA		Under the conditions of the study, the product tested is a **Skin Sensitizer**

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
SHORT TERM			
28-day dermal toxicity study, Lot: 970211/4 Pale Purple powder (99.7% purity)	CD rats(5/sex/group) at dose levels of 0, 75, 400 or 1000 mg/kg bw/day for 6 hours/day	NOAEL not established LOAEL = 75 mg/kg bw/day	**≥ 75 mg/kg bw/day:** ↓BWG, ↑Met-Hb (♂) ≥ **400 mg/kg bw/day**: ↑Met-Hb (♀) **1000 mg/kg bw/day**: ↓MCV, adrenal cortex vacuolation (♂), Histology examinations were limited and failed to include several organs considered to be targets of toxicity noted in other studies. Only 5 animals/sex/dose used. **Supplemental**
28-day Dietary Lot: FCF/T/73 White powder (94.3% purity)	Crl:CD (SD) BR rats (10/sex/group) 0, 20, 160, 1280 and 10280 ppm (equivalent to 0, 2.1, 16.7, 136.0, and 1131.0 mg/kg bw/day and 0, 2.2, 17.0, 137.0, and 1072.0 mg/kg bw/day in males and females respectively	NOAEL/LOAEL not established	**≥2.1 mg/kg bw/day**: ↓albumin, ↓P, ↑ globulin, ↑ (abs & rel.) adrenal Wt (♂) **≥16.7/17 mg/kg bw/day**: ↓Na, ↓ abs. brain Wt, (♂); ↓abs. ovary Wt, ↑(abs & rel.) Spleen Wt, (♀) **≥ 1131/1072 mg/kg bw/day**: ↑ bwg, ↑ fc;↑(abs & rel.) Spleen Wt (♂);↓ P, hemolytic anaemia (♀) **Supplemental:** Incomplete histopathology examination.
90-day dietary Lot: FCF/T/90-90 White powder (Purity not stated) (Ammannati, 1993)	Crl:CD(SD)IGS BR rats (10/sex/group) 0, 50, 100, 200 and 400 ppm (equivalent to 0, 3.5, 6.9, 13.0, and 27.8 mg/kg bw/day and 0, 4.4, 8.6, 17.5 and 34.4 mg/kg bw/day in males and females respectively)	NOAEL/LOAEL not established	**≥9 mg/kg bw/day**:↓ RBC, Hct, Hb, ↑ haematopoiesis & red pulp pigment (spleen) **(♀)** **≥13/18 mg/kg bw/day**: ↑ haemosiderin (liver); ↑haematopoiesis (spleen) (♂) **28/35 mg/kg bw/day**: ↑ (abs. 8-11%) spleen wt; hemolytic anaemia**(♀)**. Histology, haematology and clinical chemistry examinations were limited and failed to include several organs considered to be targets of toxicity noted in other studies. Test material purity not reported. **Supplemental**

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
90-day dietary Lot: 031068069, Purple tinted powder (99.5% purity) (East, 1998)	Crl:CD BR rats (10/sex/group) 0, 50, 100, 10000 or 20000 ppm (0, 4.2, 8.3, 818.5 and 1666.9 mg/kg bw/day and 0, 4.7, 8.9, 871.0 and 1820.6 mg/kg bw/day in males and females respectively)	**LOAEL =10000 ppm(818.5/871.0 mg/kg bw/day)** **NOAEL =100 ppm (8.3/8.9 mg/kg bw/day)**	**≥4.2/4.7 mg/kg bw/day**: *extramedullary erythropoiesis (spleen); haemosiderosis (spleen)* (♀) **≥8.9 mg/kg bw/day:** *↓ RBC, Hct, Hb* (♀); **≥819/871 mg/kg bw/day**: ↓ RBC, Hb , MCHC, ↑MCV, Met-Hb, Retic; ↓ Hct, ↑ (abs. & rel. 31-33%) spleen Wt, ↑ haematopoiesis, Kupffer cell pigmentation (liver) **(♀)**; haemosiderosis (spleen) (♂) **≥1667/1821 mg/kg bw/day:** ↑ (abs. & rel. 19-41%) spleen Wt (♂), ↓brain Wt (rel. 8%) **(♀)**
90-day dietary Lot: FCF/T/73 White powder (94.3% purity) (Kirk, 1990)	Crl:CD BR rats (10/sex/group) 0, 10, 320 and 10000 ppm (0, 0.7, 22.2 and 713 mg/kg bw/day and 0, 0.8, 24.3 and 754 mg/kg bw/day (♂/♀), respectively)	NOAEL/LOAEL not established	**≥22 mg/kg bw/day**: ↑WBC, thymus congestion, (abs.) kidney Wt (♂) **≥713/754 mg/kg bw/day**: hemolytic anaemia, ↓ MCHC, ↑MCV, Met-Hb, Retic, extramedullary erythropoiesis (spleen), ↑ (abs. & rel. 18-25%) spleen Wt; ↑WBC,↓(abs. & rel.) kidney Wt (♀) Histology examinations were limited and failed to include several organs considered to be targets of toxicity noted in other studies. **Supplemental**
90-day dietary Lot: 031068069 Pale Purple powder (99.8% purity) (East, 1998)	CD-1 mice (12/sex/group) 0, 30, 100, 1000 or 10000 ppm (0, 4.2, 12.8, 135.9 and 1391.9 mg/kg/day and 0, 4.7, 15.2, 135.6 and 1493.1 mg/kg bw/day in males and females respectively	**LOAEL = 100 ppm (12.8/15.2 mg/kg bw/day (♂/♀))** **NOAEL = 30 ppm (4.2/4.7 mg/kg bw/day (♂/♀)).**	**≥12.8/15.2 mg/kg bw/day**: ↑Inclusion bodies, bilirubin; ↑sulph-Hb, (♂); ↓ RBC, Hct, Hb (♀) **≥136 mg/kg bw/day:** ↑ (abs. & rel. 29-56%) spleen Wt & swollen spleens; ↓ RBC, Hct, ↑pilo-erection and ungroomed coat, ↑hepatocyte hypertrophy (♂); ↑sulph-Hb (♀) **1493 mg/kg bw/day:** ↑ (abs.) heart Wt, (♀)

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
12-month capsule "RIMON" Technical (99.3% purity)	Beagle dogs (4/sex/group) 0, 10, 100, 1000 mg/kg bw/day for 52 weeks	**LOAEL = 100 mg/kg bw/day** **NOAEL= 10 mg/kg bw/day**	**≥10 mg/kg bw/day**: */brown pigment (liver) (♂); ↑ Kupffer cell pigmentation* (♀) **≥100 mg/kg bw/day:** ↓ MCHC, ↑MCV, retic, ↑sulph-Hb, ↑Met-Hb, Heinz bodies, Howell Jolly bodies, ↑ (abs. & rel. 39-126%) spleen Wt, engorged sinusoids, red pulp congestion (spleen); ↓ RBC, Hct, Hb, ↑brown pigment (liver) (♀); hemolytic anaemia, ↑ Kupffer cell pigmentation (♂) **1000 mg/kg bw/day:** 1 (♀) mortality (firm spleen, thickened gall bladder and stomach glandular mucosa among numerous observable lesions prior to death); ↑bwg, hemolytic anaemia, Kupffer cell pigmentation; ↑bilirubin (♀)
CHRONIC TOXICITY/ONCOGENICITY			
18-month dietary (98.7% purity) Lot: 970211/4 Pale Purple powder	CD-1 mice (51 /sex/group) 0, 30, 450 or 7000 ppm (0, 3.6, 53.4 and 800.0 mg/kg/day or 0, 4.3, 63.3 and 913.4 mg/kg/day in males and females respectively	LOAEL = 450 ppm (53.4/63.3 mg/kg bw/day) NOAEL = 30 ppm (3.6/4.3 mg/kg bw/day)	**≥53/63 mg/kg bw/day:** ↑BWG, hemolytic anaemia, MCHC, ↑MCV, Met-Hb, Retic, Heinz bodies, refractile bodies, extrusion bodies, swollen spleens, ↑ extramedullary haemosiderosis & haematopoiesis (spleen); congested spleens (♂); ↑ (abs. & rel 160 - 241%) spleen Wt, liver Wt, ↓ adrenal Wt, (♀) **800/913 mg/kg bw/day**: Kupffer cell pigmentation, ↑ sulph-Hb; congested spleens, ↓ coroid pigment of adrenal (♀), No evidence of treatment related neoplasms.

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
2-year dietary Lot: 970211/4 Pale Purple powder (99.3% purity)	Rat-Sprague-Dawley (52/sex/group) 0, 25, 700, and 20000 ppm in diet 0, 1.1, 30.6, 884.2 mg/kg bw/day or 0, 1.4, 39.5, 1113.5 mg/kg bw/day males and females respectively	LOAEL: 884.2/39.5 mg/kg bw/day NOAEL: 30.6/1.4 mg/kg bw/day	**≥1.1/1.4 mg/kg bw/day** - *↑MCHC (♀); ↓MCHC (♂)* **≥31/40 mg/kg bw/day** - ↑Met-Hb, MCV, ↑spleen hemosiderosis, cortical tubule pigment (kidney); hemolytic anaemia, ↑platelet, ↑Howell-Jolly Bodies,↑retic,↑rel liver wt, ↑(abs. & rel. 31-32%) spleen wt, interstitial nephritis, proteinaceous casts, liver congestion (♀); *↑liver periacinar hypertrophy, (♂).* **884/1114 mg/kg bw/day**- ↑bwg, Heinz Bodies, ↑abs. kidney, ↑abs liver, ↑ senile nephropathy; Kupffer cell pigmentation (♀);↑FC, hemolytic anaemia, ↑retic, Howell-Jolly Bodies, ↑(abs. 16%) spleen wt, liver periacinar hepatocyte hypertrophy (♂). No evidence of treatment related neoplasms.

STUDY	SPECIES/STRAIN AND DOSES	NOEL/NOAEL and LOEL mg/kg bw/day	TARGET ORGAN/ SIGNIFICANT EFFECTS/ COMMENTS
REPRODUCTION / DEVELOPMENTAL TOXICITY			
Reproductive Toxicity RIMON Technical (99.3% purity)	CD rats,(28/sex/group) in diet at 0, 1000, 4000 or 12,000 ppm (0, 74.2/84.0, 297.5/336.7, 894.9/1009.8 mg/kg bw/day for F0 males and females respectively) and (0, 97.8/108.5, 390.2/432.5, 1182.6/1306.8 mg/kg bw/day for F1 males and females respectively).	Maternal LOAEL = 1000 ppm (74.2 mg/kg bw/day) NOAEL < 1000 ppm Offspring LOAEL = 1000 ppm (74.2 mg/kg bw/day) NOAEL < 1000 ppm Reproductive: LOAEL = 4000 ppm (297.5 mg/kg bw/day ♂) NOAEL =1000 ppm (74.2 mg/kg bw/day**)**	**Parental:** **≥74/84 mg/kg bw/day:** ↑bwg, spleen wt (F0, F1 ♂,♀ (15-39%)) **≥390/433 mg/kg bw/day**: ↑bwg, (F1♀); ↑kidney wt (F1 ♂) **895/1010 mg/kg bw/day:** ↑kidney wt (F0 ♂, F1♀), ↑haemosiderosis (spleen) (F0/1 ♂, F0/1♀), ↑hepatocyte hypertrophy (F1 ♂) **Offspring:** **≥74/84 mg/kg bw/day**: ↑ mean litter pup bw at birth (F1 &f2), ↓ pup bwg during lactation, ↓ litter wt during lactation (F1 & F2) ↑spleen wt (9-18%), liver wt (F1/2 ♂,♀), delayed sexual maturation (F1 ♂). **Reproductive:** **≥297 mg/kg bw/day:**↓ epididymal sperm count, (F1 ♂).
Developmental toxicity CD Rats Lot: 970211/4 Pale Purple powder (99.3% purity)	CD rats (22 mated groups), dosed by gavage at 0, 250, 500 or 1000 mg/kg bw/day in 0.5% carboxymethylcellulose from days 6 through 15 of gestation	Maternal NOAEL = 1000 mg/kg bw/day Developmental NOAEL = 1000 mg/kg bw/day	There were no adverse effects of treatment noted in this study. **Not teratogenic**
Developmental toxicity Rabbit Lot: 970211/4 Pale Purple powder (99.1% purity)	New Zealand White rabbits (22 mated groups), dosed by gavage at 100, 300 or 1000 mg/kg bw/day in 0.5% carboxymethylcellulose from Day 6 to 19 of gestation	Maternal NOAEL = 1000 mg/kg bw/day Developmental NOAEL = 1000 mg/kg bw/day	**≥300 mg/kg bw/day**: */incompletely ossified 5th sternebrae (Non-adverse)* There were no adverse effects of treatment noted in this study. **Not teratogenic**

STUDY	SPECIES and STRAIN or CELL TYPE AND CONCENTRATIONS or DOSES		RESULTS
GENOTOXICITY			
Gene mutations in bacteria (93.5% purity)	*Salmonella typhimurium* strains TA 98, TA 100, TA 1535, 1538 and TA 1537; 10, 33, 100, 333, 1000 or 3333 µg/plate; with and without activation		**Negative**
Gene mutations in bacteria (99.3% purity)	*Salmonella typhimurium* strains TA 98, TA 100, TA 1535, 1538 and TA 1537; *E. Coli (WP2 uvr A*) 0, 312.5, 625, 1250, 2500 or 5000 µg/plate; with and without activation		**Negative**
Bacteria DNA Repair Assay (99.3% purity)	H17 and M45 (Bacillus subtilis); 0, 50, 150, 500, 1500 or 5000 µg/plate; with and without activation		Although no clear dose-response, survival index ratios for the 2 highest doses were <.75. **Equivocal.**
Gene mutations in mammalian cells (*in vitro*) (94.3% purity)	Mouse Lymphoma Assay (TK locus) 0, 50, 100, 125, 150, 175 and 200 µg/mL without activation 0, 50, 100, 125, 150, 175 and 200 µg/mL with activation		**Negative**
Unscheduled DNA synthesis *(/n vitro)* (94.3% purity)	Human HeLa S3 Epithelioid cells 0, 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, 32, 64, 128 or 256 µg/mL (cultures scored for UDS 180 minutes after dose administration)		**Negative**
Micronucleus assay (*in vivo*) (94.3% purity)	Male and female CD-1 (ICR) mice 0, 1250, 2500 or 5000 mg/kg (single oral dose; bone marrow harvested 24, 48 and 72 hours post-dosing)		No mortalities. Clinical signs of toxicity such as piloerection, hunched posture, pallor of extremities **Negative**
SPECIAL STUDIES (if applicable)			
Acute Neurotoxicity (99.3% purity)	Crl:CD(SD)IGS BR rats (10/sex/group) 0, 200, 650, or 2000 mg/kg bw by gavage in 1.0% carboxymethylcellulose	NOAEL = 2000 mg/kg bw (♂,♀)	Low incidences of clinical signs including vocalization, fast respiration and irritable behaviour resolved by day 5 post-dosing. **Not neurotoxic**
Subchronic Neurotoxicity Lot: 970211/4 Pale Purple powder (99.5% purity)	Crl:CD(SD)IGS BR rats (10/sex/group) in diet 0, 50, 200, 2000 and 20000 ppm (equivalent to 0, 17.5, 174 and 1752 mg/kg bw/day and 0, 20.5, 207 and 2000 mg/kg bw/day in males and females respectively)	NOAEL = 1752/2000 mg/kg bw/day (♂,♀)	There were no adverse effects of treatment noted in this study. **Not neurotoxic**

Compound-Induced Mortality:
In the 12-month dog study there was a single high dose female death attributed to treatment at a daily dose of 1000 mg/kg bw/day. The animal displayed indications of overt toxicity prior to death (firm spleen, thickened gall bladder and stomach glandular mucosa among numerous observable lesions prior to death).
In the multi-generation reproductive toxicity study, there was increased pup death observed in both the F1 and F2 generations during lactation.

Recommended ARD: There are no end-points indicating toxicity following a single exposure to the test material. As a result, an acute reference dose is not being set for this test compound.

Recommended ADI: The Acceptable Daily Intake is set from the 90-day feeding study in mice. The NOAEL was 4.2 mg/kg bw/day, based on increases in inclusion bodies, bilirubin and sulph-Hb, with associated decreases in RBC parameters at the LOAEL of 12.8/15.2 mg/kg bw/day. The effect noted in RBCs is considered the salient end point in the database. There did not appear to be a durational effect noted for this endpoint, with the severity of blood turn over not progressing in severity with prolonged dosing. As a result, the NOAEL identified in the 90-day mouse study is considered to be protective for chronic exposure to the chemical. The ADI is derived by dividing the NOAEL by the typical 10 * 10 factors to account for intra and inter species variability. Thus, the ADI is 4.2 mg/kg bw/day /100 = 0.042 mg/kg bw/day.

Tox Endpoints for Occupational Risk Assessment:
Thus, for all short-to-intermediate exposure scenarios the 28-day dermal toxicity study was chosen for end-point selection. The LOAEL was 75 mg/kg bw/day based on adverse haematological effects and reduced body weight gain in males. The standard 100x SF/UF is applied for interspecies/intraspecies variation, while an additional 3x is applied for the use of a LOAEL.

Table 3.5.2 Integrated Food Residue Chemistry Summary

Nature of the Residue in Apple			Reference: 686930
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron	
Test Site	Outdoor plot		
Treatment	2 foliar applications at 110-day, 90-day before harvest **or** 3 applications at 110-day, 90-day and 60-day before harvest		
Rate	25 - 27 g a.i./ha/applc. (52-78 g a.i./ha/season)		
End-use product	RIMON 10 EC		
Preharvest interval	*2 foliar applications:* 0 (samples collected following each application), 30, 60 and 90 days *3 foliar applications:* 0 (samples collected following each application), 30 and 60 days		
The majority of the radioactivity in the treated fruits were recovered in the surface washes, accounting for 85% of the TRR (0.067 - 0.080 ppm) after the third application (for both labels). Significant portion of the absorbed radioactivity was found in the peel of the fruit, accounting for 13 - 46% TRR (0.005 - 0.025 ppm), with very low levels of radioactivity observed in the flesh (1 - 7% TRR; ≤0.003 ppm). Translocation study indicated that radioactive residues did not translocate from foliage into fruits.			
Metabolites identified	Major metabolites (>10% TRR)		Minor metabolites (<10% TRR)	
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron
Fruit: ACN wash	Novaluron	Novaluron	None	None
Fruit: peel	Novaluron	Novaluron	None	None
Fruit: flesh	None	None	None	None
Leaves	Novaluron	Novaluron	None	None

Nature of the Residue in Potato			Reference: 686933
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron	
Test Site	Outdoor plot containing sandy loam soil		
Treatment	2 foliar applications at 70- and 84-day post-planting		
Rate	100 g a.i./ha/applc. (200 g a.i./ha/season)	91 and 98 g a.i./ha/applc. (189 g a.i./ha/season)	
End-use product	RIMON 10 EC		
Preharvest interval	0 (samples collected following each application), 7, 19 and 29 days		
Total radioactive residues ranged from nondetectable to 0.001 ppm in mature potato tubers and from 0.785 to 9.87 ppm in potato foliage. No further analytical work was conducted on potato tubers. Translocation of radioactive residues from foliage into potato tubers is not evident.			
Metabolites identified	Major metabolites (>10% TRR)	Minor metabolites (<10% TRR)	

Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron
Foliage	Novaluron	Novaluron	None	None
Tubers	None	None	None	None
Nature of the Residue in Cabbage				Reference: 686931
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron		[Chlorophenyl-^{14}C(U)] Novaluron	
Test Site	Outdoor plot containing sandy loam soil			
Treatment	*42-day PHI*: 2 foliar applications at 56- and 42-day before harvest *14-day PHI*: 2 foliar applications at 35- and 14-day before harvest			
Rate	*42-day PHI* 34 - 41 g a.i./ha/applc. (75 g a.i./ha/season) *14-day PHI* 30 - 40 g a.i./ha/applc. (70 g a.i./ha/season)		*42-day PHI* 37 - 45 g a.i./ha/applc. (82 g a.i./ha/season) *14-day PHI* 35 - 38 g a.i./ha/applc. (73 g a.i./ha/season)	
End-use product	RIMON 10 EC			
Preharvest interval	*42-day PHI*: 0 (samples collected following each application), 14, 28 and 42 days *14-day PHI*: 0 (samples collected following each application), 7 and 14days			
The majority of the radioactivity in treated cabbage at final harvest (PHI of 14 or 42 days) was recovered in the surface washes, accounting for 81.9 - 97.7% of the TRR (0.192-1.024 ppm).				
Metabolites identified	Major metabolites (>10% TRR)		Minor metabolites (<10% TRR)	
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron
ACN wash	Novaluron	Novaluron	None	None
Leaves	Novaluron	Novaluron	None	None
Nature of the Residue in Cotton				Reference: 686915
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron		[Chlorophenyl-^{14}C(U)] Novaluron	
Test Site	Outdoor plot containing loamy sand			
Treatment	*Regime 1*: 2 foliar applications at 104- and 90-day before harvest *Regime 2*: 2 foliar applications at 44- and 30-day before harvest			
Rate	47 - 59 g a.i./ha/applc. (95-110 g a.i./ha/season)		43 - 51 g a.i./ha/applc. (87-104 g a.i./ha/season)	
End-use product	RIMON 10 EC			
Preharvest interval	*Regime 1*: 0 (samples collected following each application), 30, 60 and 90 days *Regime 2*: 0 (samples collected following each application), 30 days			

The TRR were 0.148-1.12 ppm in gin byproducts and <0.01 ppm in undelinted seed. Results from the translocation experiment indicate that the radioactivity detected in protected bolls collected at final harvest after 2 applications was low (0.001 - 0.002 ppm) suggesting that translocation within the plant is minimal.

Metabolites identified	Major metabolites (>10% TRR)		Minor metabolites (<10% TRR)	
Radiolabel	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron	[Difluorophenyl-^{14}C(U)] Novaluron	[Chlorophenyl-^{14}C(U)] Novaluron
Gin by-products	Novaluron	Novaluron	None	None
Undelinted seed	None	None	None	None

Confined Rotational Crop Study - Spinach, Turnip and Spring wheat	Reference: 883987
Radiolabel	[Chlorophenyl-^{14}C(U)] Novaluron
Test Site	Plants grown in plastic containers (containing sandy loam soil) maintained in an environmentally controlled room with nominal temperature set at 15ºC and diurnal light cycle control set at 11 hr/light, 13 hr/dark gradually increased to 16 hr/light, 8 hr/dark
Treatment	Radiolabel was applied once to soil; rotational crops were planted 30 days and 120 days after soil treatment
Rate	93.8 g a.i./ha/season
End-use product	10 EC

Preharvest interval

(Days post-planting)

	immature	*earliest harvest*	*final harvest*
Spinach	35	68	102
Turnip	35	69	97
Wheat	55 (forage)	133 (hay)	165 (grain & straw)

The results from the confined crop rotational study carried out with diverse crops, namely turnip (root and tuber), spinach (leafy vegetable) and spring wheat (cereal) indicate that uptake of radioactive novaluron, which had been aged in the soil for 30 days, by the rotational crops was negligible.

Nature of the Residue in Lactating Goat			Reference: 686932
Species	**Radiolabel**	**Dose Level**	**Sacrifice**
Capra hircus	[Difluorophenyl-^{14}C(U)] Novaluron	0.417 mg/kg bw/day (12.3 ppm in feed)	23 hours after the last dose
	[Chlorophenyl-^{14}C(U)] Novaluron	0.423 mg/kg bw/day (10.6 ppm in feed)	23 hours after the last dose

Radioactive residues in collected goat matrices were adequately extracted with methanol or methanol:water. In the difluorophenyl label study, 92.6-100% of TRR (0.079-1.374 ppm) in milk and tissues were extractable. In the chlorophenyl label study, 93.8-99.5% of TRR (0.079-1.92 ppm) in milk and tissues were extractable. Nonextractable residues accounted for 0-7% of TRR (0-0.032 ppm).

Metabolites identified	Major metabolites (>10% TRR)		Minor metabolites (<10% TRR)	
Radiolabel	Difluorophenyl-^{14}C	Chlorophenyl-^{14}C	Difluorophenyl-^{14}C	Chlorophenyl-^{14}C
Liver	Novaluron	Novaluron	2,6-difluorobenzoic acid	1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy) phenyl]urea
Kidney	Novaluron	Novaluron	2,6-difluorobenzoic acid	None
Fat (peritoneal)	Novaluron	Novaluron	None	None
Muscle (fore-leg)	Novaluron	Novaluron	None	None
Milk	Novaluron	Novaluron	None	None

Therefore, the residue definition in ruminant animal products may be defined as novaluron only for enforcement and risk assessment purposes. The metabolism of novaluron in ruminant animals is adequately documented.

Crop Field Trials-Pome Fruits (Apple and Pear)	Reference: 581138, 800013, 800014, 883990 and 1103007

A total of 22 field trials on apple and 10 field trials on pear were submitted. With the exception of one field trial on apple, the number and geographic location of these trials satisfied the Canadian requirements for apple and pear. The field trials were carried out using a 6.7% and/or 7.5% water-dispersible granule formulation of novaluron in accordance with the use pattern described in the proposed Canadian label (application rate of 2.1 kg a.i./ha/season and a PHI of 14 days) and are acceptable.

Since the field trials were conducted using a formulation (7.5WDG) that is different from the petitioned product (10EC), the applicant submitted additional side-by-side field trials (5 on apple; 2 on pear) to compare the residue profile. The results showed that residue profiles generated from both formulation types were similar. Therefore, residue data generated with the WDG formulation are considered acceptable to reflect the use of the petitioned product (10EC formulation).

Commodity	**Total Rate kg a.i./ha**	**PHI (days)**	**Novaluron Residue Levels (ppm)**						
			n	**Min.**	**Max.**	**HAFT**	**Median**	**Mean**	**SD**
Concentrate Spray (421 - 606 L/ha):									
Apple	2.234-2.326	13-15	43	0.195	1.149	1.06	0.589	0.617	0.225
Dilute Spray (3394 - 3811 L/ha):									
Apple	2.248-2.256 (3.034*)	14	8	0.242	0.557	0.522	0.421	0.408	0.100

* One trial received a higher rate due to mixing error; residues from this trial were within the residue range of the others.

Commodity	Total Rate kg a.i./ha	PHI (days)	Novaluron Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	SD
Concentrate Spray (438 - 513 L/ha):									
Pear	2.221-2.284	14	20	0.177	1.95	1.79	0.703	0.879	0.555
Dilute Spray (3488 - 3844 L/ha):									
Pear	2.248-2.252	14	4	0.424	0.807	0.785	0.595	0.606	0.208
Formulation Bridging Study (7.5WDG and 10EC): side-by-side trials (5 apple trials and 2 pear trials)									
Apple & Pear (7.5WDG)	1.076	14	14	0.196	0.824	0.761	0.394	0.446	0.176
Apple & Pear (10EC)	1.076	14	14	<0.050	1.260	1.110	0.359	0.475	0.325

Crop Field Trials-Potato	Reference: 883984, 883985 and 883986

A total of 20 crop field trials on potato were submitted: 18 trials were conducted in Europe (EU); 2 trials were conducted in the United States (U.S.). Out of the 2 U.S. trials, one was carried out in the Canadian requested region of Zone 1, the other was in a U.S. requested region of Zone 11.

Commodity	Total Rate g a.i./ha	PHI (days)	Novaluron Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median	Mean	SD
Potato	571.1 - 577.5	7	4	<0.05	<0.05	<0.05	<0.05	<0.05	--
	50.0 - 57.4	21/22	18	<0.01	<0.01	<0.01	<0.01	<0.01	--

Residue Decline- Pome Fruits	Reference: 800013 and 800014

Both residue trials were carried out in the applicable apple and pear growing region of Zone 11.

Commodity	Rate g a.i./ha	PHI (days)	Novaluron Residue Levels (ppm)	
			Residue	Average
Apple	2259	0	0.8390, 1.0400	0.94
		3	0.6660, 0.9090	0.788
		7	0.5410, 0.6860	0.614
		14	0.5890, 0.5980	0.594
		28	0.7200, 0.7730	0.747
Pear	2221	0	0.6310, 0.8550	0.743
		3	0.5550, 0.6700	0.613
		7	0.4830, 0.5320	0.508
		14	0.3980, 0.4380	0.418
		28	0.2570, 0.2980	0.278

Residue Decline- Potato	Reference: 883985 and 883986

Results generated from 8 residue decline trials carried out in Europe showed that residues of novaluron in/on potato tubers harvested at PHI 0, 3, 7, 14 and 21 days were all below LOQ.

Processing Studies - Apple	Reference: 800013 and 800014

Novaluron, formulated as 6.7% water-dispersible granule (WDG) containing 6.7% w/w active ingredient, was applied to apple plants with six broadcast foliar applications at a rate of 374 - 376 g a.i./ha/application for a total rate of 2252 g a.i./ha/season (1.1-fold the proposed maximum label rate).

Fraction	**Novaluron Residue levels (ppm)**	**Calculated Concentration factor**
Apple, RAC	0.405	---
Wet Pomace	2.91	7.2
Juice	<0.05	<0.1

Storage Stability - Plant Matrices	Reference: 883981, 883982, 883983 and 883990

Matrix	Demonstrated Storage		Actual Maximum Storage	
	Duration (months)	Temperature	Duration (months)	Temperature
Apple	12	-18ºC	5.7	<0ºC
Pear	5.2	<0ºC	5.1	<0ºC
Potato	12	-18ºC	6.9	<0ºC
Apple Juice	3.3	<0ºC	3.1	<0ºC
Apple Pomace	NT	NT	3.2	<0ºC
Broccoli	6	-18ºC	---	---
Cabbage	7	-18ºC	---	---
Tomato	12	-18ºC	---	---
Orange Wet Pomace	7.8	-18ºC	---	---
Orange Dry Pomace	7.6	-18ºC	---	---
Orange Marmalade	8	-18ºC	---	---
Orange Peel	7.6	-18ºC	---	---

NT = Not tested. Although there is no data to demonstrate the freezer storage stability of novaluron in apple wet pomace, there is data showing that novaluron residues are stable under frozen conditions for 3.3 months in the processed commodity of apple juice and for at least 6 months in orange matrices (wet pomace, dry pomace, peel and marmalade).

Storage Stability - Animal Matrices

In the cow feeding study, samples of milk and animal tissue including muscle, liver, kidney and fat were frozen within 24 hours of collection, and were processed and analyzed within 30 days of being taken. Therefore, no freezer storage stability information is needed.

Livestock Feeding	Reference: 681466

Lactating cattle (Friesian, *Bos taurus*) were administered 0.44 ppm, 3.86 ppm, 12.57 ppm and 42.83 ppm novaluron for 42 days. The maximum theoretical dietary burden (MTDB) for beef and dairy cattle are 8.3 ppm and 4.4 ppm, respectively. The depuration study indicates that residues of novaluron generally decreased with cessation of dosing; however, quantifiable residues remained in milk and tissues collected up to 36 days following the last dose from the 3.86 ppm and 42.83 ppm dose levels.

Matrix	Maximum Residue Levels (ppm) of Novaluron by Feeding Level				
	7 mg a.i./day (0.44 ppm in feed)	53 mg a.i./day (3.86 ppm in feed)	159 mg a.i./day (12.57 ppm in feed)	530 mg a.i./day (42.83 ppm in feed)	Anticipated Residue
Whole milk	0.06	0.17	0.43	2.07	0.0865
Cream	1.12	3.06	7.66	20.9	0.9387
Skimmed milk	<0.01	0.02	0.04	0.14	0
Muscle	0.05	0.09	0.34	0.56	0.0554
Kidney	0.06	0.14	0.35	1.2	0.1075
Liver	0.05	0.14	0.41	1.36	0.1239
Subcutaneous Fat	0.43	1.24	4.36	8.21	Not used
Peritoneal Fat	0.56	2.25	6.83	12.89	1.1827

Table 3.5.3 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT **Primary crops (apple, potato, cabbage,cotton)** **Rotational crops (turnip, wheat, spinach)**	 Novaluron Novaluron
METABOLIC PROFILE IN DIVERSE CROPS	The profile is similar in the apple, potato, cabbage and cotton metabolism studies.
ANIMAL STUDIES	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT	Novaluron
METABOLIC PROFILE IN ANIMALS (goat)	Only goat was investigated.
FAT SOLUBLE RESIDUE	Yes
WATER	
RESIDUE DEFINITION FOR RISK ASSESSMENT ONLY The most pronounced toxicological effects associated with novaluron exposure in water are thought to be associated with the chloroaniline metabolite. Environmental degradates containing the chloroanaline moiety have the potential to reach drinking water sources. Chlorophenyl urea is more mobile and persistent in soil than novaluron, and may have the potential to reach surface water through runoff at levels equal to, or greater than, novaluron. Chlorophenyl urea shares similar toxicity as novaluron.	Novaluron + Metabolite 275-352I (chlorophenyl urea): 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy ethoxy) phenyl]urea + Metabolite 275-309I (chloroaniline): 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy ethoxy)aniline

DIETARY RISK FROM FOOD AND WATER					
Chronic Non-Cancer Dietary Risk **ADI = 0.042 mg/kg bw/day** **EEC= 3 µg a.i./L (novaluron)** **0.035 µg a.i./L (275-352I)** **65.9 µg a.i./L (275-309I)** Metabolite 275-352I (chlorophenyl urea): 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy ethoxy) phenyl]urea Metabolite 275-309I (chloroaniline): 3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxy ethoxy)aniline	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**			
		Food (Refined)	**Refined: Food + Water (EEC)**		
			novaluron	**275-352I**	**275-309I**
	All infants < 1 yr old	**6.5**	**7.0**	**6.5**	**17.3**
	Children 1 to 2 yrs	**10.0**	**10.2**	**10.0**	**14.9**
	Children 3 to 5 yrs	**7.8**	**8.0**	**7.8**	**12.4**
	Children 6 to 12 yrs	**4.4**	**4.6**	**4.4**	**7.6**
	Youth 13 to 19 yrs	**2.1**	**2.2**	**2.1**	**4.5**
	Adults 20 to 49 yrs	**1.7**	**1.8**	**1.7**	**4.8**
	Adults 50+ yrs	**1.6**	**1.8**	**1.6**	**4.9**
	Females 13 to 49 yrs	**1.6**	**1.8**	**1.6**	**4.7**
	Total Population	**2.6**	**2.8**	**2.6**	**5.9**

Appendix II Supplemental Maximum Residue Limit (MRL) Information - International Situation and Trade Implications

Three of the proposed Canadian MRLs are the same as those in the U.S. In seven cases, the MRLs differ from the MRLs established in the US (http://www.access.gpo.gov/nara/cfr/waisidx_04/40cfr180_04.html).

Table 1 Differences Between Canadian MRLs and Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Milk, fat	8	20	Not reviewed by Codex
Fat of cattle, goat, horse and sheep	7	11	
Milk	0.5	1	
Liver and kidney of cattle, goat, horse and sheep	0.4	1	
Meat and meat byproducts (except liver and kidney) of cattle, goat, horse and sheep	0.4	0.6	
Hog, fat	0.01	0.05	
Liver and kidney of hog	0.01	Not established	

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

The differences in MRLs for animal commodities between Canada and the U.S. listed in Table 1 are due to different livestock feed items and practices. There is an extra use on cotton in the U.S.

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 proposed in this regulatory amendment 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.

Appendix III Crop Groups: Numbers and Definitions

Crop Group Number	Name of the Crop Group	Commodity
11	Pome fruit	Apples Crabapples Loquats Mayhaws Pears Oriental pears Quinces
1C	Tuberous and corm vegetable	Arracaha Arrowroot Chinese Artichokes Jerusalem Artichokes Edible Canna Cassava Roots Chayote Roots Chufa Ginger Roots Lerens Potatoes Sweet Potato Roots Tanier Corms Taro Corms Turmeric Roots Yam Bean Roots True Yam Tubers

Table 4.1 Fate and Behaviour in the Environment

Study Type	Test Substance	Study Conditions	Value	Major Transformation Products[1]	Reference
Soil					
Phototransformation	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluorophenyl labels)	25°C, continuous irradiation Sandy loam (pH 5.4, %OM 1.8)	First order half-life (Equivalent days at mid-summer 40°N) dark: >60 days (>15 days unconverted) irradiated: no trend evident ($r^2 < 0.5$) First order half-life (Equivalent days on October 27 52°N and 0°W) dark: >172 (>15 days unconverted) irradiated: no trend evident ($r^2 < 0.5$)	None	PMRA #686888
Aerobic metabolism	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluorophenyl labels)	Clay loam (pH 8.8, %OM 1.7); Sandy loam (pH 5.8, %OM 0.8); Silt loam (pH 7.0, %OM 3.7)	First order half-life 20°C: 6.9-14 days 10°C: 22 days Curvilinear DT_{50}: 20°C: 4-12 days* 10°C: 21 days* Curvilinear DT_{90}: 20°C: >120 days 10°C: >120 days *The curvilinear DT_{50} better represented the data.	275-352I and CO_2* *38% of the applied radioactivity after 30 days in the pilot study with the ^{14}C-difluorophenyl label	PMRA #686912, #686916
	275-352I	Test substance was novaluron parent. 275-352I was the major transformation product. No separate study was submitted.	First order half-life 20°C: 25-54 days Curvilinear DT_{50}: 20°C: 14-23 days* Curvilinear DT_{90} 20°C: 65 to >113 days *The curvilinear DT_{50} better represented the data.	N/A	PMRA #686912, #686916

Study Type	Test Substance	Study Conditions	Value	Major Transformation Products[1]	Reference
Anaerobic metabolism	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluoro-phenyl labels)	Loamy (pH 6.3, %OC 4.5); Sandy loam (pH 6.2, %OC1.7)	First order half-life: 37-55 days Curvilinear DT_{50}: 35-45 days* Curvilinear DT_{90} 181-183 days *The curvilinear DT_{50} better represented the data	275-352I (14-32%, 2-9 Months) 275-309I (5.8-50%, 6 -12 Months) 275-158I (94% 12 Months)	PMRA #686893
Adsorption/ Desorption	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluoro-phenyl labels)	Clay loam (pH 7.1, %OC 1.9); Sandy loam (pH 5.8, %OC 0.8); Sandy loam (pH 6.4, %OC 2); Silt loam (pH 6.0, %OC 2.4)	K_{oc}: 6030 - 11828* *Based on simple adsorption coefficient	N/A	PMRA #686911
	^{14}C-275-352I	Loamy sand (pH 6.0, %OC 2.4); Sandy loam (pH 5.8, %OC 1.8); Sandy loam (pH 5.8, %OC 0.8); Clay loam (pH 7.1, %OC1.9)	K_{oc}: 1951 - 2528	N/A	PMRA #686910

Study Type	Test Substance	Study Conditions	Value	Major Transformation Products[1]	Reference
Soil leaching	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluoro-phenyl labels)	Unaged Soil	Negligible residues were detected beyond the 5 cm depth and leachates (<3.2 and <0.9% respectively).	N/A	PMRA #686892
	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluoro-phenyl labels) and 275-352I	Aged Soil Note: Test substance was novaluron parent. 275-352I was the major transformation product. No separate study was submitted.	0-8 cm: <67.2% detected 8-33 cm: <5.5% detected Leachates: <1.4% detected CO_2: 20.9% detected	275-352I	PMRA #686889
Volatilization	Novaluron		Vapour pressure: 1.6 x 10^{-5} Pa at 25^{o}C Henry's law constant: H = 2.628 Pa*m^{3}*mol^{-1} at 20^{o}C H = 2.59 × 10^{-5} atm*m^{3}*mol^{-1} at 20^{o}C 1/H = 962.8 at 20^{o}C		PMRA #293623

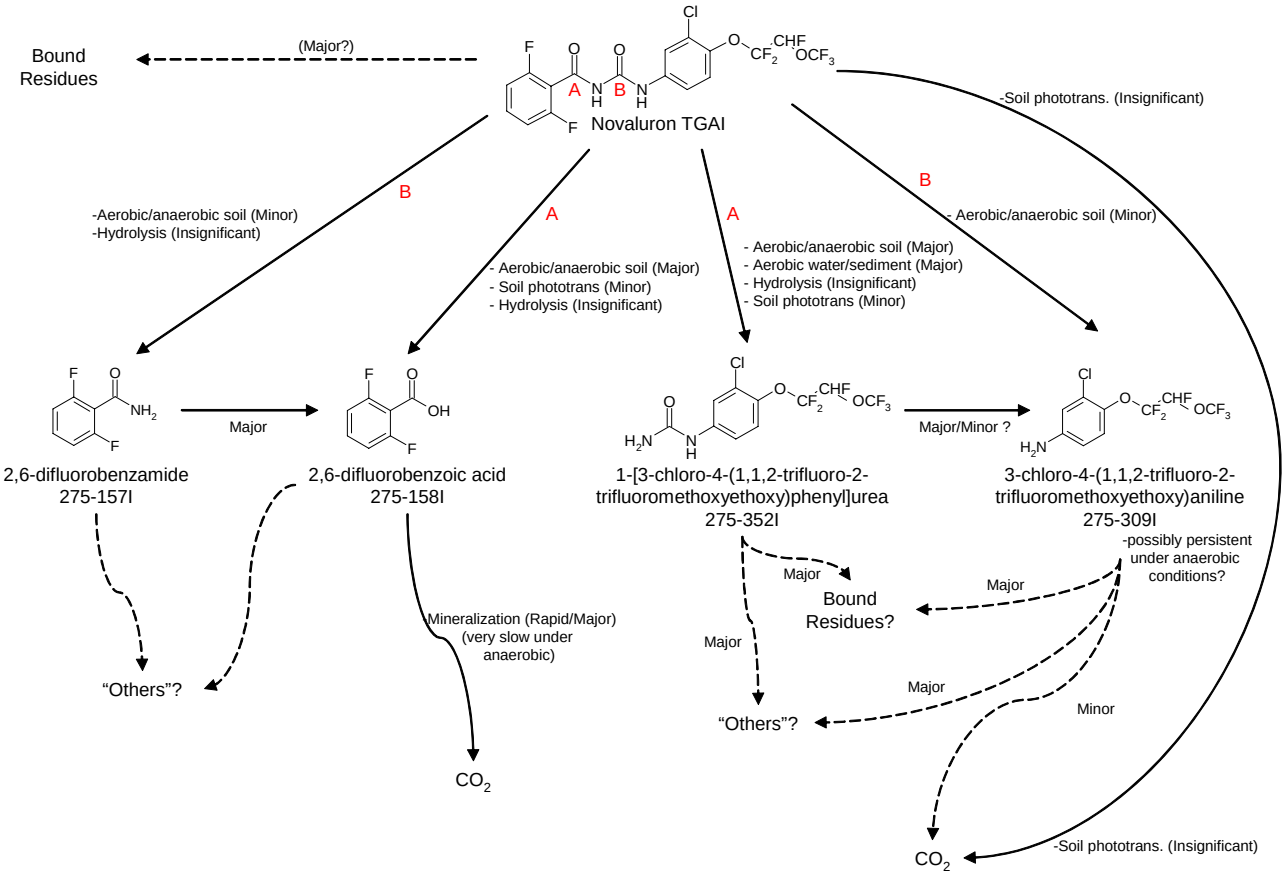
Study Type	Test Substance	Study Conditions	Value	Major Transfor-mation Products[1]	Reference
Field dissipation	Novaluron (non-radiolabelled)	Studies conducted in Nova Scotia, Ontario, New York, and Washington	Nova Scotia: Curvelinear DT_{50}: 81 days Curvelinear DT_{75}: 103 days Curvelinear DT_{90}: >4 months Expected Carryover: 3.9% Expected time to steady state: 1 year Ontario: Curvelinear DT_{50}: 18 days Curvelinear DT_{75}: 61 days Curvelinear DT_{90}: >5 months Expected Carryover: 1.6% Expected time to steady state: <1 year New York: Curvelinear DT_{50}: 62 days Curvelinear DT_{75}: >5.5 months Curvelinear DT_{90}: >5.5 months Expected Carryover: 8.7% Expected time to steady state: 2 years Washington: Curvelinear DT_{50}: 38 days Curvelinear DT_{75}: >5.5 months Curvelinear DT_{90}: >6 months Expected Carryover: 0.54% Expected time to steady state: <1 year		PMRA #686887

Study Type	Test Substance	Study Conditions	Value	Major Transformation Products[1]	Reference
Aquatic systems					
Hydrolysis	Novaluron	25°C (pH 5, 7, and 9)	Stable at all three pH	275-158I* *Presence should be considered only as qualitative evidence for transformation, as the quantization is suspect.	PMRA #686890
Phototransformation	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluorophenyl labels)	25°C, continuous irradiation, sterile water (pH 5)	First order half-life (Equivalent days at mid-summer 40°N) dark: Expected to be >60 days irradiated: no trend evident ($r^2 < 0.5$) First order half-life (Equivalent days on October 27 52°N and 0°W) dark: Expected to be >172 days irradiated: no trend evident ($r^2 < 0.5$)	275-157I (24%)* *Presence should be considered only as qualitative evidence for transformation, as the quantization is suspect.	PMRA #686891

Study Type	Test Substance	Study Conditions	Value	Major Transformation Products[1]	Reference
Aerobic water/ sediment metabolism	Novaluron (^{14}C-chlorophenyl and ^{14}C-difluoro-phenyl labels)	20°C Pond water pH 7.7 Sediment (clay-loam) %OC 1.0; Pond water pH 7.4-7.7 Sediment (loamy sand) %OC 1.4	Water: First order half-life: 0.9-1.3 days Curvilinear DT_{50}: 0.8-1.3 days Curvilinear DT_{90}: 4.5-8 days Sediment: First order half-life: 8.2-28 days Curvilinear DT_{50}: 4-23 days Curvilinear DT_{90}: 28-95 days System: First order half-life: 6.3-26 days Curvilinear DT_{50}: 9.4-22 days Curvilinear DT_{90}: 29-90 days	275-352I (18-22% Day 14-30) CO_2 (47% Day 30)	PMRA #686913
Anaerobic metabolism	See Anaerobic flooded soil				PMRA #686893

[1] Unless otherwise noted, parentheses represent maximum concentrations [as % of the applied] and time [days] to maximum concentration.

Figure 4.1 Transformation Pathway for Novaluron in the Environment



-No transformation product contained both rings
-Others – various polar and other transformation products, none exceeding 5% of applied radioactivity

Table 4.2 Toxicity to Non-Target Species

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
Terrestrial Organisms					
Mammals	Rat	Acute Oral	Novaluron	NOEC: 5000 mg a.i./kg bw LD_{50}: >5000 mg a.i./kg bw	PMRA #686934
		90-day Dietary	Novaluron	NOAEC: 100 mg a.i./kg diet LOAEC: 10000 mg a.i./kg diet (blood effects, increased spleen weight)	PMRA #686970
		Reproductive study 2-generation	Novaluron	NOAEC: <1000 mg a.i./kg diet LOAEC: 1000 mg a.i./kg diet (Offspring effects: increased pup mortality, increased body weight at birth, decreased body weight gain during lactation, increased spleen and liver weight, delayed sexual maturation; Parental effects: increased body weight gain and spleen weight)	PMRA #686907
	Mouse	90-day Dietary	Novaluron	NOAEC: 30 mg a.i./kg diet LOAEC: 100 mg a.i./kg diet (blood effects)	PMRA #686939
Birds	Bobwhite quail	Acute Oral (single dose; 14-day observation)	Novaluron	LD_{50}: >2000 mg ai/kg bw NOEC: 2000 mg ai/kg bw	PMRA #686882
		Dietary (5-day exposure; 3-day post-exposure)	Novaluron	5-day LC_{50}: >5200 mg ai/kg dw diet LOEC (based on mortality): 5200 mg ai/kg dw diet NOEC: 2610 (2600 nominal) mg ai/kg dw diet	PMRA #686954
		Reproduction (dietary exposure 10 week pre-laying; 12 week laying)	Novaluron	$NOEC_{repro}$: 300.7 (300 nominal) mg ai/kg diet $LOEC_{repro}$: 1010 (1000 nominal) mg ai/kg diet; based on decreased eggs laid/pen, eggs laid/female, 14-day survivors/hatchlings, 14-day survivors/female $NOEC_{parent}$: 1010 mg ai/kg diet $LOEC_{parent}$: >1010 mg ai/kg diet (note: body weight gain was observed among treated adults)	PMRA #686885
	Mallard duck	Acute Oral (single dose; 14-day observation)	Novaluron	LD_{50}: >2000 mg ai/kg bw NOEC: 2000 mg ai/kg bw	PMRA #686953
		Dietary (5-day exposure; 3-day post-exposure)	Novaluron	5-day LC_{50}: >5310 mg ai/kg dw diet NOEC: 5310 mg ai/kg dw diet	PMRA #686955

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
		Reproduction (dietary exposure 10 week pre-laying; 12 week laying)	Novaluron	$NOEC_{repro}$: 30 mg ai/kg diet $LOEC_{repro}$: 50.7 mg ai/kg diet; based on decreased eggs laid/pen, eggs laid/female, 14-day survivors/female $NOEC_{parent}$: 50 mg ai/kg diet $LOEC_{parent}$: >50 mg ai/kg diet (note: body weight gain was observed among treated adults)	PMRA #686886
Bee	*Apis mellifera*	48-hour Acute Oral	Novaluron	48-hour NOEC: 100 µg ai/bee 48-hour LD_{50}: >100 µg ai/bee	PMRA #686952
		48-hour Acute Contact	Novaluron	48-hour NOEC: 100 µg ai/bee 48-hour LD_{50}: >100 µg ai/bee	PMRA #686952
		48-hour Acute Oral	Rimon 10EC	48-hour NOEC: 200 µg EP/bee (18.2 µg a.i./bee) 48-hour LD_{50}: >200 µg EP/bee (>18.2 µg a.i./bee)	PMRA #883998
		48-hour Acute Contact	Rimon 10 EC	48-hour NOEC: 200 µg EP/bee (18.2 µg a.i./bee) 48-hour LD_{50}: >200 µg EP/bee (>18.2 µg a.i./bee)	PMRA #883998
		Brood/hive -semi field: Hive exposed to 1L of 50% sucrose feeding solution containing 3.3 mL EP/L. Bees consumed the test substance within 63 hours, and then foraged freely on natural sources for remainder of 21-day test period.	Rimon 10 EC	Hive consumed 1 L of 3.3 mL EP/L sucrose solution: effects on brood development (egg, young larvae, old larvae development)	PMRA #883999
		Brood/hive -field: Hives exposed to flowering citrus trees sprayed at 2 x 225 g ai/ha, 7 day interval. Brood development monitored over 24 days in field; and then hive monitored for an additional month.	Rimon 10 EC	450 g ai/ha cumulative application (7 day interval): Effects on brood development (egg, young larvae, old larvae development)	PMRA #884000

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
Terrestrial arthropods (including beneficial predators and parasites)	Including beneficial predators and parasites	Field study: Natural populations of terrestrial arthropods exposed to 2 x 225 g ai/ha (7 day interval) applied to citrus trees.	Rimon 10 EC	470 g ai/ha cumulative application (7day interval): Effects on parasitic wasp emergence from aphids (no effect beyond two days post-application) and predatory mite nymph populations (recovery in ~2 months of application)	PMRA #799971
Earthworm	*Eisenia foetida*	14-day Acute	Novaluron	14-day NOEC 1000 mg a.i./kg dw soil (highest test concentration) 14-day LOEC: >1000 mg a.i./kg dw soil 14-day LC_{50}: >1000 mg a.i./kg dw soil	PMRA #686884
			275-352I	14-day NOEC: 171 mg a.i./kg dw soil 14-day LOEC: 309 mg a.i./kg dw soil (effects: mortality, body weight loss) 14-day LC_{50}: 447 mg a.i./kg dw soil	PMRA #686883

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
Vascular Plants	6 dicots and 4 monocots	Seedling emergence	Rimon 10 EC	NOEC: 15 g a.i./ha (maximum concentration tested) Note: chlorosis and reduced crop vigour were observed in sunflower; symptoms were transient Note: Because the maximum test concentration was 15 g a.i./ha, the study is not acceptable to assess plant toxicity for the proposed use rates, which are much higher.	PMRA #686986
		Vegetative vigour	Rimon 10 EC	NOEC: 15 g a.i./ha (maximum concentration tested) [Note: chlorosis and reduced crop vigour were observed in sunflower; symptoms were transient] Note: Because the maximum test concentration was 15 g a.i./ha, the study is not acceptable to assess plant toxicity for the proposed use rates, which are much higher.	PMRA #686986
Freshwater Organisms					
Invertebrates	*Daphnia magna*	48-hr Acute	Novaluron TGAI (Measured: 0.2, 0.30, 0.46, 0.66, 0.72, 1.07 µg a.i./L)	EC_{50} = 0.31 µg a.i./L NOEC = 0.20 µg a.i./L LOEC = 0.31 µg a.i./L	PMRA #686968
			275-352I (Measured: 0.32, 0.69, 1.6, 3.5, 7.48 mg a.i./L)	EC_{50} = 1.85 µg/L** NOEC = 1.60 µg/L LOEC = 3.50 µg/L**	PMRA #686964
			Rimon 10 EC (9.1% Novaluron) (Measured: 0.26, 0.34, 0.56, and 1.1 µg a.i./L)	EC_{50} = 5.9 µg EP/L NOEC = <2.88 µg EP/L LOEC = 2.88 µg EP/L Equivalent to: EC_{50} = 0.54 µg a.i./L NOEC = <0.26 µg a.i./L LOEC = 0.26 µg a.i./L	PMRA #983514

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
		21-day Chronic	Novaluron TGAI (Measured: 3.8, 6.9, 14.5, 29.9, 62.8 ng a.i./L)	EC_{50} = 46.8 ng a.i./L** NOEC = 29.9 ng a.i./L LOEC = 62.8 ng a.i./L**	PMRA #686962
Fish	Rainbow trout	96-hr Acute	Novaluron TGAI (Measured: 0.95 mg a.i./L)	LC_{50} > 0.95 mg a.i./L NOEC = 0.95 mg a.i./L LOEC > 0.95 mg a.i./L	PMRA #686936
			275-352I (Measured: 0.14, 0.22, 0.67, 1.4, 2.7 mg/L)	LC_{50} = 0.51 mg/L NOEC = <0.144 mg/L LOEC = 0.144 mg/L	PMRA #686961
			Rimon 10 EC (9.1% Novaluron) (Measured as a.i.: 0.24, 0.49, 1.0, 1.8, 3.9, 8.3 mg a.i./L)	LC_{50} = 62.7 mg EP/L NOEC = 5.4 mg EP/L LOEC = 11.0 mg EP/L Equivalent to: LC_{50} = 5.7 mg a.i./L NOEC = 0.49 mg a.i./L LOEC = 1.0 mg a.i./L	PMRA #884010
		Chronic (28-day prolonged)	Novaluron TGAI (Measured: 6.5 µg a.i./L - Highest tested concentra-tion; no observable effects were noted)	LC50 > 6.5 µg a.i./L NOEC = 6.5 µg a.i./L LOEC = >6.5 µg a.i./L	PMRA #686967
			Rimon 10 EC (9.1% Novaluron) (Measured: 0.11, 0.31, 0.63, 1.8, 4.4 mg a.i./L)	LC50 = 6.9 mg EP/L NOEC = 1.2 mg EP/L LOEC = 3.4 mg EP/L Equivalent to: EC50 = 0.63 mg a.i./L NOEC = 0.11 mg a.i./L LOEC = 0.31 mg a.i./L	PMRA #884011

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
	Bluegill sunfish	Acute	Novaluron (Measured: 0.95 mg a.i./L)	LC_{50} > 0.95 mg a.i./L NOEC = 0.95 mg a.i./L LOEC > 0.95 mg a.i./L**	PMRA #686937
		Bioaccumulation	Novaluron (Measured: 0.05, 0.521 µg a.i./L)	0.05 µg a.i./L: Elimination rate constant k_2 (1/days) = 0.0552 r^2 = 0.981 Bioconcentration Factor (BCF) = 14220x Elimination first order half-life (days) = 12.55 days First order DT_{90} (days) = 41.72 days 0.521 µg a.i./L: Elimination rate constant k_2 (1/days) = 0.579 r^2 = 0.9858 Bioconcentration Factor (BCF) = 15260x Elimination first order half-life (days) = 11.97 days First order DT_{90} (days) = 39.78 days	PMRA #686963
Amphibians	Rainbow trout use as surrogate	Acute and chronic rainbow trout data were used.			PMRA #686936, #686961, #884010
Algae	Green algae	*S. capriconutum* 96-hour Acute	Novaluron (Measured: 9.85 mg a.i./L)	NOEC = 9.85 mg a.i./L EC_{50} > 9.85 mg a.i./L	PMRA #686969
			Rimon 10 EC (9.1% Novaluron) (Measured: 0.92, 2.4, 6.0, 13.9, 30.1, 69.4 mg a.i./L	EC50 = 43 mg EP/L (biomass)** EC50 = 48 mg EP/L (growth rate)** EC50 = 41 mg EP/L (cell density)** NOEC = 27 mg EP/L LOEC = 66.2 mg EP/L** Equivalent to: EC50 = 3.9 mg a.i./L (biomass)** NOEC = 2.4 mg a.i./L LOEC = 6.0 mg a.i./L **	PMRA #884013
			275-352I (Measured: 49, 104, 209, 436, 890 µg/L)	EC50 = 325 µg/L (biomass) NOEC = 104 µg/L LOEC = 209 µg/L	PMRA #686965
Plant	*Lemna gibba*	14-day Acute	Rimon 10 EC (Measured: 75.4 µg a.i./L)	EC50 = >777 µg EP/L NOEC = 777 µg EP/L LOEC = >777 µg EP/L Equivalent to: EC50 > 75.4 µg a.i./L NOEC = 75.4 µg a.i./L LOEC > 75.4 µg a.i./L	PMRA #686966

Organism	Species	Study Type	Test Substance	Toxicity Data*	Reference
Microcosm Study	Freshwater pelagic and benthic inverte-brates, algae, macrophytes	21-week study; at study initiation novaluron applied 2 times at 14-day intervals	Novaluron (Nominal concentra-tions of 0.05, 0.15, 0.5, 1.5, 5.0 µg a.i./L)	Community NOEC: 0.05 µg a.i./L (Effects with recovery on pelagic nauplii and cyclopods; complete elimination of benthic gammarids with no recovery)	PMRA #884006
Estuarine/Marine Organisms					
Invertebrates	Mysid shrimp	96-hour Acute	Novaluron TGAI (Measured: 28, 42, 79, 160, 207 ng a.i./L)	EC50 = 0.14 µg a.i./L** NOEC = 0.079 µg a.i./L LOEC = 0.16 µg a.i./L**	PMRA #686985
		28-day Chronic	Novaluron TGAI (Measured: 7.3, 13.5, 26.1, 59.1, 116 ng a.i./L)	EC50 = 0.099 µg a.i./L (mortality)** NOEC = 0.059 µg a.i./L LOEC = 0.12 µg a.i./L**	PMRA #686983
	Eastern oyster	28-day Chronic	Novaluron TGAI (Measured: 0.18, 0.23, 0.52, 1.24, 1.64 µg a.i./L)	EC50 = 1.4 µg a.i./L (Shell growth) NOEC = 0.23 µg a.i./L LOEC = 0.52 µg a.i./L	PMRA #686924
Fish	Sheepshead minnow	Acute	Novaluron TGAI (Measured: 0.23, 0.44, 0.80, 1.3, and 2.0 µg a.i./L)	LC50 > 2.0 µg a.i./L NOEC = 2.0 µg a.i./L LOEC = >2.0 µg a.i./L	PMRA #686984

* In many cases, no effects were seen up to the limit of solubility for the chemical (for aquatic toxicity tests).

** LOECs were determined using ANOVA. LC/EC_{50} were determined using either Probit Analysis or Trimmed Spearman-Karber methods. In many cases, the slope of the mortality curve resulted in an EC_{50} or LC_{50} that was less than the LOEC.

Table 4.3 Deterministic risk assessment for terrestrial organisms[1].

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
Terrestrial Vertebrates—all food obtained from treated field without dissipation of active substance					
Mammals	Acute oral (Rat)	Novaluron	NOEC: 5000 mg a.i./kg bw (highest dose tested; no observable effects were noted)	Apple/Pear: 1059 mg a.i./kg dw diet	28 days[1]
				Potato: 89 mg a.i./kg dw diet (cumulative)	330 days[1]
	90-day Dietary (Rat)	Novaluron	NOAEC: 100 mg a.i./kg diet LOAEC: 10000 mg a.i./kg diet (blood effects, incresed spleen weight)	Apple/Pear: 1059 mg a.i./kg dw diet (deterministic)	10.5 (0.105 using the LOAEC)
				Potato: 89 mg a.i./kg dw diet (cumulative)	0.89 (0.0089 using the LOAEC)
	Reproductive - 2 generation (Rat)	Novaluron	NOAEC: <1000 mg a.i./kg diet (LOAEC: 1000 mg a.i./kg diet)	Apple/Pear: 1059 mg a.i./kg dw diet	1
				Potato: 89 mg a.i./kg dw diet	0.09
	90-day Dietary (Mouse)	Novaluron	NOAEC: 30 mg a.i./kg diet LOAEC: 100 mg a.i./kg diet (blood effects)	Apple/Pear: 1053 mg a.i./kg dw diet (deterministic)	35.1 (10.5 using the LOAEC)
				Potato: 88 mg a.i./kg dw diet (cumulative)	2.9 (0.88 using the LOAEC)
Bobwhite Quail	Acute 14- day Oral: (Bobwhite Quail)	Novaluron	NOEL: 2000 mg a.i./kg bw (highest dose tested; no observable effects were noted)	Apple/Pear: 368 mg a.i./kg dw diet	97 days[1]
				Potato: 30.8 mg a.i./kg dw diet	1158 days[2]
	Acute 5-day Dietary: Novaluron TGAI (Bobwhite Quail)	Novaluron	NOEC: 2610 mg a.i./kg diet	Apple/Pear: 368 mg a.i./kg dw diet	0.141
				Potato: 30.8 mg a.i./kg dw diet	0.0118

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
	Reproduction (Bobwhite Quail)	Novaluron	NOEC: 300.7 mg a.i./kg diet	Apple/Pear: 368 mg ai/kg dw diet (deterministic)	1.22
				Potato: 30.8 mg a.i./kg dw diet	0.102
	Acute 14-day Oral (Mallard Duck)	Novaluron	NOEL: 2000 mg a.i./kg bw (highest dose tested; no observable effects were noted)	Apple/Pear: 71 mg a.i./kg dw diet	31 days[1]
				Potato: 6.0 mg a.i./kg dw diet	367 days[1]
	Acute 5-day Dietary (Mallard Duck)	Novaluron	NOEC: 5310 mg ai/kg diet (highest dose tested; no observable effects were noted)	Apple/Pear: 71 mg a.i./kg dw diet	0.013
				Potato: 6.0 mg a.i./kg dw diet	0.001
	Reproduction (Mallard Duck)	Novaluron	NOEC: 30 mg a.i./kg diet	Apple/Pear: 71 mg a.i./kg dw diet	2.37 (cumulative)
				Potato: 6.0 mg a.i./kg dw diet	0.2

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
Terrestrial Invertebrates—contact exposure to treated surfaces or ingestion of a treated sucrose solution (arthropods), or exposure to treated soil (earthworms)					
Bees	Acute 48 hr Oral	Novaluron	NOEC: 112 kg a.i./ha (converted from 100 µg a.i./bee)	Apple/Pear: 525 g a.i./ha (single)	0.0047
				Potato: 88 g a.i./ha (single)	0.00078
	Acute 48 hr Contact	Novaluron	NOEC: 112 kg a.i./ha (converted from 100 µg a.i./bee)	Apple/Pear: 525 g a.i./ha (single)	0.0047
				Potato: 88 g a.i./ha (single)	0.00078
	Acute 48 hr Oral:	Rimon 10 EC (9.1% Novaluron)	NOEC: 224 kg EP/ha (converted from 200 µg EP/bee)	Apple: 5769 g EP/ha (single) (525 g a.i./ha)	0.025
				Potato: 967 g EP/ha (single) (88 g a.i./ha)	0.0043
	Acute 48 hr Contact:	Rimon 10 EC (9.1% Novaluron)	NOEC: 224 kg EP/ha (converted from 200 µg EP/bee)	Apple: 5769 g EP/ha (single) (525 g a.i./ha)	0.025
				Potato: 967 g EP/ha (single) (88 g a.i./ha)	0.0043
Earthworms	Acute	Novaluron	NOEC: 1000 mg a.i./kg dw soil (highest dose tested; no observable effects were noted)	Apple/Pear: 0.824 mg a.i./kg soil	0.00082
				Potato: 0.075 mg a.i./kg soil	0.00008
		275-352I	NOEC (weight): 171 mg/kg soil	Apple/Pear: 0.589 mg/kg soil	0.00344
				Potato: 0.0537 mg/kg soil	0.00031
Terrestrial Vascular Plants—exposure to direct overspray					
Vascular plants	Seedling emergence and vegetative vigour	Novaluron	Toxicity and to terrestrial plants at the proposed application rates could not be fully assessed based on the submitted data (see text).		

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
Freshwater Organisms—exposure to water body of 30-cm depth directly oversprayed*					
Inverte-brates	Acute (*Daphnia magna*)	Novaluron	NOEC: 200 ng a.i./L	Apple/Pear: 0.490 mg a.i./L	2450
				Potato: 0.0518 mg a.i./L	259
		275-352I**	NOEC: 1.6 µg/L	Apple/Pear: 0.351 mg/L	219
				Potato: 0.0371 mg/L	23
		275-352I***	NOEC: 1.6 µg/L	Apple/Pear: 0.077 mg/L	48
				0.0081 mg/L	5.1
		Rimon 10 EC (9.1% Novaluron)	NOEC: <2.88 µg EP/L (<0.26 µg a.i./L) (Lowest concentration tested)	Apple/Pear: >5.38 mg EP/L (0.490 mg a.i./L)	>1868
				Potato: >0.569 mg EP/L (0.0518 mg a.i./L)	198
	Chronic (*Daphnia magna*)	Novaluron	NOEC: 29.9 ng a.i./L (Reduced fecundity)	Apple/Pear: 0.490 mg a.i./L	16388
				Potato: 0.0518 mg a.i./L	1732
Fish	Acute (Rainbow Trout)	Novaluron	NOEC: 0.95 mg a.i./L (Highest tested concentration; no observable effects were noted)	Apple/Pear: 0.490 mg a.i./L	0.52
				Potato: 0.0518 mg a.i./L	0.054
		275-352I**	NOEC: <0.144 mg/L (Lowest concentration tested)	Apple/Pear: >0.351 mg/L	>2.4
				Potato: >0.0371 mg/L	>0.26
		275-352I***	NOEC: <0.144 mg/L (Lowest concentration tested)	Apple/Pear: >0.077 mg/L	>0.54
				Potato >0.0081 mg/L	>0.057

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
		Rimon 10 EC (9.1% Novaluron)	NOEC: 5.4 mg EP/L (0.49 mg a.i./L)	Apple/Pear: 5.38 mg EP/L (0.490 mg a.i./L)	1
				Potato: 0.569 mg EP/L (0.0518 mg a.i./L)	0.1
	Prolonged 28-day (Rainbow Trout)	Novaluron	NOEC: 6.5 µg a.i./L (Highest tested concentration; no observable effects were noted)	Apple/Pear: 0.490 mg a.i./L	75
				Potato: 0.0518 mg a.i./L	8
		Rimon 10 EC (9.1% Novaluron)	NOEC: 1.2 mg EP/L (0.11 mg a.i./L) Behavioural effects noted	Apple/Pear: 5.38 mg EP/L (0.490 mg a.i./L)	4.5
				Potato: 0.569 mg EP/L (0.0518 mg a.i./L)	0.47
	Acute (Bluegill Sunfish)	Novaluron	NOEC: 0.95 mg a.i./L (Highest tested concentration; no observable effects were noted)	Apple/Pear: 0.490 mg a.i./L	0.52
				Potato: 0.0518 mg a.i./L	0.054
Amphibians	Acute (Rainbow Trout used as surrogate)	Rimon 10 EC (9.1% Novaluron)	NOEC: 5.4 mg EP/L (0.49 mg a.i./L)	Apple/Pear: 5.38 mg EP/L (0.490 mg a.i./L)	1
	Prolonged 28-day (Rainbow Trout used as sur-rogate)	Novaluron	NOEC: 6.5 µg a.i./L (Highest tested concentration; no observable effects were noted)	Apple/Pear: 0.490 mg a.i./L	75
				Potato: 0.0518 mg a.i./L	8
		Rimon 10 EC (9.1% Novaluron)	NOEC: 1.2 mg EP/L (0.11 mg a.i./L) Behavioural effects noted	Apple/Pear: 5.38 mg EP/L (0.490 mg a.i./L)	4.5
				Potato: 0.569 mg EP/L (0.0518 mg a.i./L)	0.47
Microcosm	Two applications, 14-day intervals (Various community species and taxa)	Novaluron	NOEC: 0.05 µg a.i./L Community (Benthic and pelagic invertebrates)	Apple/Pear: 0.490 mg a.i./L	9800
				Potato: 0.0518 mg a.i./L	1036

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
Algae	Acute	Novaluron	NOEC: 9.8 mg a.i./L (Highest concentration tested; no observable effects were noted)	Apple/Pear: 0.490 mg a.i./L	0.05
				Potato: 0.0518 mg a.i./L	0.0053
		Rimon 10 EC (9.1% Novaluron)	NOEC: 27 mg EP/L (2.45 mg a.i./L) Biomass affected	Apple/Pear: 5.38 mg EP/L (0.490 mg a.i./L)	0.2
				Potato: 0.569 mg EP/L (0.0518 mg a.i./L)	0.021
		275-352I**	NOEC: 104 µg/L Biomass affected	Apple/Pear: 0.351 mg/L	3.38
				Potato: 0.0371 mg/L	0.36
		275-352I***	NOEC: 104 µg/L Biomass affected	Apple/Pear: 0.077 mg/L	0.74
				Potato: 0.0081 mg/L	0.078
Vasclular Plant	Acute (*Lemna minor*)	Rimon 10 EC	NOEC: 777 µg EP/L (70.7 µg a.i./L)	Apple/Pear: 5.38 mg EP/L (0.490 mg a.i./L)	6.9
				Potato: 0.569 mg EP/L (0.0518 mg a.i./L)	0.73
Estuarine/Marine Organisms—exposure to water body of 30-cm depth directly oversprayed*					
Inverte-brates	Acute (*Mysidopsis bahia*)	Novaluron	NOEC: 79 ng a.i./L	Apple/Pear: 0.490 mg a.i./L	6202
				Potato: 0.0518 mg a.i./L	656
	Prolonged 28-day (*Mysidopsis bahia*)		NOEC: 26.1 ng a.i./L Mean terminal male length affected	Apple/Pear: 0.490 mg a.i./L	18774
				Potato: 0.0518 mg a.i./L	1984
	Prolonged 28-day (Eastern Oyster)	Novaluron	230 ng a.i./L Shell deposition affected	Apple/Pear: 0.490 mg a.i./L	2130
				Potato: 0.0518 mg a.i./L	225

Organism	Study Type	Test Substance	Toxicity	Exposure	RQ
Fish	Acute (Sheepshead minnow)	Novaluron	NOEC: 2.0 µg a.i./L (Highest concentration tested; no observable effects were noted))	Apple/Pear: 0.490 mg a.i./L	245
				Potato: 0.0518 mg a.i./L	26

[1] Apple/Pear Orchard Use: Expected Environmental Concentration (EEC) and Risk Quotient (RQ) based on a cumulative application rate (4 x 525 g a.i./ha, 10 day interval), or where indicated, a single application (525 g a.i./ha).
Potato Use): EEC and RQ based on a cumulative application rate (2 x 88 g a.i./ha, 10 day interval), or where indicated, a single application rate (88 g a.i./ha).

[2] Number of days of continuous consumption required to attain the dose equivalent to that administered in the laboratory that had no-observable effect on the laboratory population.

* Expected environmental concentration based on an aerobic water/sediment whole system first order half-life of 26 days.

**Based on a 100% conversion from novaluron to 275-352I.

***Based on a 22% conversion from novaluron to 275-352I, determined from the aerobic water/sediment study.

[redacted] - When RQ is greater than one, a refined RA is done.

Table 4.4 Refined Risk Assessment on Non-Target Species*

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
Terrestrial Vertebrates					
Mammals	90-day Dietary (Rat)	Novaluron	NOAEC: 100 mg a.i./kg diet	The screening level assumes no dissipation of product from foliage/food items between applications. More realistic to consider a single application rate, which assumes dissipation will occur between applications, washoff, new plant growth, and transformation. The corresponding refined EEC is 265 and 44 mg a.i./kg dw diet, respectively, for apple/pear and potato applications.	Risk quotient values are 2.6 and 0.44, respectively, for apple/pear and potato applications. Mortality is not expected from dietary consumption and the populations of mice or rats near an orchard are not likely to be impacted by dietary exposure to this chemical (see text). Therefore, the dietary exposure of mice or rats in orchards was not considered to be a significant concern. No further mitigation is required.
	90-day Dietary (Mouse)	Novaluron	NOAEC: 30 mg a.i./kg diet	As above. The corresponding refined EEC is 265 and 44 mg a.i./kg dw diet, respectively, for apple/pear and potato applications.	Risk quotient values are 8.8 and 1.5, respectively, for apple/pear and potato applications. Mortality is not expected from dietary consumption and the populations of mice or rats near an orchard are not likely to be impacted by dietary exposure to this chemical (see text). Therefore, the dietary exposure of mice or rats in orchards was not considered to be a significant concern. No further mitigation is required.
	Repro-ductive 2-gener-ation (Rat)	Novaluron	NOAEC: <1000 mg a.i./kg diet (LOAEC: 1000 mg a.i./kg diet)	As above. The corresponding refined EEC is 265 and 44 mg a.i./kg dw diet, respectively, for apple/pear and potato applications.	Risk quotient values are 0.26 and 0.044, respectively, for apple/pear and potato applications; no further mitigation is required.

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
Birds	Repro-ductive (Bob-white Quail)	Novaluron	NOEC: 300.7 mg a.i./kg diet	As above. The corresponding refined EEC is 92 and 15 mg a.i./kg dw diet, respectively, for apple/pear and potato applications.	Risk quotient values are 0.30 and 0.050, respectively, for apple/pear and potato applications; no further mitigation is required.
	Repro-ductive (Mallard Duck)	Novaluron	NOEC: 30 mg a.i./kg diet	As above. The corresponding refined EEC is 18 and 3 mg a.i./kg dw diet, respectively, for apple/pear and potato applications.	Risk quotient values are 0.6 and 0.1, respectively, for apple/pear and potato applications; no further mitigation is required.
Freshwater Aquatic Organisms					
Inverte-brates	Acute (*Daphnia magna*)	Novaluron	NOEC: 200 ng a.i./L	**Spray Drift Assessment:** The screening level assumes 100% drift to a water body. The maximum drift deposition on bare ground expected at one metre downwind from the point of application is 74 and 6%, respectively, for apple/pears (early airblast) and potatoes (ground spray). The cor-responding EECs are 0.363 and 0.00318 mg a.i./L	Risk quotient values are 1815 and 16, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: The screening level assumes 100% drift to a water body and is available for biological uptake, regardless of the physico-chemical properties, especially the solubility limit. More realistic to consider risk at the solubility limit ans free-swimming organisms are not expected to be exposed to concentrations beyond this value. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 17. Further refinement is necessary.

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
			NOEC: 200 ng a.i./L	**Runoff Assessment:** Determine the geographic areas where the major crop (apple) is grown. Pick the scenario that generates the highest EEC for marine exposure (apple orchard in Nova Scotia), assuming 10% drift. The 90th percentile of the peak predicted concentration in water, as a result of runoff, after pesticide application is 1.64 and 0.77 µg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 8.2 and 3.8, respectively, for apple/pear and potato applications. Therefore, risks remain. Buffer zones have been calculated based on the **chronic** *Daphnia* endpoint as it is the most sensitive freshwater indicator. Appropriate label hazard statements have been added to the product label.
	Chronic (*Daphnia magna*)	Novaluron	NOEC: 29.9 ng a.i./L Reduced fecundity	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L for apple/pear and potato applications.	Risk quotient values are 12140 and 106, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 114. Further refinement is necessary.
				Runoff Assessment: As above. The 90th percentile of the predicted concentration in water, as a result of runoff **21 days** after pesticide application is 0.25 and 0.16 µg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 8.4 and 5.3, respectively, for apple/pear and potato applications. Therefore, risks remain. This is the most sensitive freshwater endpoint. Buffer zones larger than one metre are required to mitigate the risk. Buffer zones have been calculated and added on the label under "Directions for use". Appropriate label hazard statements have been added to the product label.

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
Fish	Pro-longed 28-day	Novaluron	NOEC: 6.5 µg a.i./L (Highest tested concentra-tion; no observable effects were noted)	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 56 and 0.49, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 0.52. No further mitigation is required.
Amphi-bians	Pro-longed 28-day (rainbow trout use as surrogate species)	Novaluron	NOEC: 6.5 µg a.i./L (Highest tested concentra-tion; no observable effects were noted)	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 56 and 0.49, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 0.52. No further mitigation is required.
Micro-cosms	Two appli-cations, 14-day intervals (Various com-munity species and taxa)	Novaluron	NOEC: 50 ng a.i./L Lowest tested concentra-tion (Benthic gammarids most sensitive with no recovery)	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 7260 and 64, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 68. Further refinement is necessary.

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
				Runoff Assessment: As above. The 90th percentile of the predicted peak concentration in sediment interstitial water, as a result of runoff after pesticide application is 113 and 77 ng a.i./L, respectively, for apple/pear and potato applications. Corresponding 90-day concentrations were 105 and 65 ng a.i./L.	Risk quotient values are 2.3 and 1.5, respectively, for apple/pear and potato applications at peak predicted concentrations. Corresponding 90-day risk quotients are 2.1 and 1.3. Therefore, risks remain. Buffer zones have been calculated based on the chronic *Daphnia* endpoint as it is the most sensitive freshwater indicator. Appropriate label hazard statements have been added to the product label.
Marine/Estuarine Aquatic Organisms					
Inverte-brates	Acute (*Mysido-psis bahia*)	Novaluron	NOEC: 79 ng a.i./L	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 4595 and 40, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 43. Further refinement is necessary.
				Runoff Assessment: As above. The 90th percentile of the peak predicted concentration in water after 96 hours, as a result of runoff after pesticide application, is 0.69 and 0.35 µg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 8.7 and 4.4, respectively, for apple/pear and potato applications. Therefore, risks remain. Buffer zones have been calculated based on the chronic *Mysid* endpoint as it is the most sensitive estuarine indicator. Appropriate label hazard statements have been added to the product label.

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
	Chronic (*Mysido-psis bahia*)	Novaluron	NOEC: 26 ng a.i./L (Terminal male length)	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 13961 and 122, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 131. Further refinement is necessary.
				Runoff Assessment: As above. The 90th percentile of the predicted concentration in water, as a result of runoff **21 days** after pesticide application is 0.25 and 0.16 µg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 9.6 and 6.1, respectively, for apple/pear and potato applications. Therefore, risks remain. Estuarine buffer zones have been calculated based on the chronic *Mysid* endpoint as it is the most sensitive indicator in marine environments. Appropriate label hazard statements have been added to the product label.
Mollusk	Pro-longed 28-day (Eastern Oyster)	Novaluron	NOEC: 230 ng a.i./L Shell deposition affected	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 1578 and 14, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 15. Further refinement is necessary.
				Runoff Assessment: As above. The 90th percentile of the predicted concentration in water, as a result of runoff **21 days** after pesticide application is 0.25 and 0.16 µg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 1.1 and 0.7, respectively, for apple/pear and potato applications. Therefore, some risks remain. Buffer zones have been calculated based on the chronic *Mysid* endpoint as it is the most sensitive estuarine indicator. Appropriate label hazard statements have been added to the product label.

Category	Study Type	Test Substance	Toxicity	Refinement	Risk Characterization
Fish	Acute (Sheeps-head Minnow)	Novaluron	NOEC: 2.0 µg a.i./L (Highest tested concentra-tion; no observable effects were noted).	**Spray Drift Assessment:** As above. The EECs are 0.363 and 0.00318 mg a.i./L, respectively, for apple/pear and potato applications.	Risk quotient values are 182 and 2, respectively for apple/pear and potatoes, respectively. Further refinement is necessary.
				Solubility Limit Assessment: As above. Solubility limit: 3.4 µg a.i./L	Risk quotient value is 1.7. Further refinement is not necessary as no adverse effects were noted.

* The spray drift did not make a significant contribution to the overall expected environmental concentration (e.g., 1.64 µg a.i./L spray drift vs. 1.60 µg a.i./L no spray drift).

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5.0 VALUE

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PMRA 884030 RIM-18-01: Determine the effective rate of novaluron 10EC against Colorado potato beetle in potatoes. DACO 10.2.3.3.

PMRA 884032 1999 U.S. Rimon Trials: Colorado Potato Beetle in Potatoes. DACO 10.2.3.3.

PMRA 884033 1999 U.S. Rimon Trials: Colorado Potato Beetle in Potatoes. DACO 10.2.3.3.

PMRA 884034 Rimon 10EC (Novaluron): A new insect growth Regulator for control of the Colorado potato beetle on potatoes. DACO 10.2.3.3.

PMRA 884037 Foliar CPB Aroostock Farm Maine, DACO 10.2.3.3.

PMRA 884038 UOGRIM - 02: Determine the effective rate of novaluron 10EC in the control of Colorado potato beetles. DACO 10.2.3.3.

PMRA 884035 DNJ03030: Evaluate novaluron 0.83EC for the control of Colorado potato beetle and leps. DACO 10.2.3.3.

PMRA 884039 POT_PTB_03: Evaluate Diamond 0.83 for control of Colorado potato beetle on potatoes grown in the Columbia Basin. DACO 10.2.3.3.

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PMRA 1114409 European corn borer control of snap bean with foliar insecticides. Arlington. DACO 10.6.

PMRA 799979 RIM-22-03: Determine the effective rate of novaluron 7.5 WDG against key lepidopterous pome fruit pests. DACO 10.2.3.3.

PMRA 799983 RIM-22-05: Determine the effective rate of novaluron 7.5 WDG against key lepidopterous pome fruit pests. DACO 10.2.3.3.

PMRA 799984 RIM-22-06: Determine the effective rate of novaluron 7.5 WDG against key lepidopterous pome fruit pests. DACO 10.2.3.3.

PMRA 1103012 MAN04I01: Efficacy of novaluron against Oriental fruit moth in apples. DACO 10.2.3.3.

PMRA 1103015 Novaluron/2004/-RIMON-02:Tolerance to, and efficacy of novaluron against codling moth and other insect pests in apples. DACO 10.2.3.3.

PMRA 1103016 2004 - RIMON - 01: Determine effective rate of different novaluron formulations against codling moth in apple. DACO 10.2.3.3.

PMRA 1286405 Efficacy: small scale trials. DACO 10.2.3.3.

B. ADDITIONAL INFORMATION CONSIDERED

ii) List of Unpublished Information Considered

3.0 IMPACT ON HUMAN AND ANIMAL HEALTH

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PMRA 1306926 [^{14}C]Rimon 10EC *in vivo* Dermal Penetration Study in the Male Rat. MKC Study No. R-11140. 20-June-00. DAC 5.8

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