Proposed Registration Decision PRD2011-12

Imazapyr

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Overview

Proposed Registration Decision for Imazapyr and Ares Herbicide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Imazapyr Technical Herbicide and Ares Herbicide, containing the technical grade active ingredient imazapyr and imazamox , to control broadleaf and grassy weeds in Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait).

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

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Imazapyr Technical Herbicide and Ares Herbicide.

What Does Health Canada Consider When Making a Registration Decision?

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

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

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

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (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 when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on imazapyr, the PMRA will consider all comments received from the public in response to this consultation document[3]. The PMRA will then publish a Registration Decision[4] on imazapyr, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

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

What Is Imazapyr?

Imazapyr is an active ingredient in the end-use product Ares Herbicide. Ares Herbicide contains the active ingredients imazapyr at 15 grams per litre and imazamox at 33 grams per litre of product. Ares is a post-emergence herbicide, i.e., a herbicide applied after weeds and crops have emerged from the ground, which is applied using ground application equipment to Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality Brassica juncea (e.g., canola quality Brassica juncea varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait) to control broadleaf and grassy weeds. Imazapyr inhibits the plant enzyme acetolactate synthase (ALS) in target weeds. Chlorosis and tissue necrosis may not be apparent in some plant species until two weeks after application.

[3] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

[4] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Imazapyr Affect Human Health?

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

Potential exposure to imazapyr may occur through the 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 uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

In laboratory animals, the technical grade active ingredient (TGAI) imazapyr was of low acute toxicity by the oral and dermal routes, but was of slight toxicity via the inhalation route. Imazapyr was non-irritating to the skin and did not cause an allergic skin reaction, but was severely irritating to the eye. Consequently, the hazard signal words “CAUTION POISON” and “DANGER – EYE IRRITANT” are required on the label.

The acute toxicity of the end-use product Ares Herbicide containing imazapyr as well as the technical imazamox was low via the oral, dermal and inhalation routes of exposure. It was minimally irritating to the eye and slightly irritating to the skin. Ares Herbicide did not cause an allergic skin reaction.

There was no indication that imazapyr caused damage to the nervous system or immune system. Imazapyr did not cause birth defects in animals and there were no effects on the ability to reproduce. There was no indication of target organ toxicity. There was no evidence to suggest that imazapyr damaged genetic material or caused cancer at doses relevant to humans. Health effects in animals given repeated doses of imazapyr over long periods of time were early deaths and decreased survivorship.

When imazapyr was given to pregnant or nursing animals, no effects on the developing fetus or juvenile animal were observed, indicating that the young are not more sensitive to imazapyr than the adult animal.

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

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and children 1-2 years old, the subpopulation which would ingest the most imazapyr relative to body weight, are expected to be exposed to 0.00% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from imazapyr is not of concern for all population sub-groups. There is no evidence that imazapyr is carcinogenic; therefore, a cancer dietary assessment is not required.

Animal studies revealed no acute health effects. Consequently, a single dose of imazapyr 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). Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada using imazapyr on Clearfield canola and Clearfield lentils were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this Consultation Document.

Occupational Risks From Handling Ares Herbicide

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

Farmers and custom applicators who mix, load or apply Ares Herbicide as well as field workers re-entering freshly treated fields can come in direct contact with imazapyr residues on the skin. Therefore, the label specifies that anyone mixing and loading Ares Herbicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves and goggles or a face shield. In addition, the label specifies that anyone applying Ares Herbicide must wear a long-sleeved shirt and long pants. The label also requires that workers do not enter treated fields for 12 hours after application. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, the risk to these individuals is not a concern.

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

Environmental Considerations

What Happens When Imazapyr Is Introduced Into the Environment?

Imazapyr poses a potential risk to non-target terrestrial plants. Therefore, risk-reduction measures including precautionary label statements and buffer zones must be observed.

The environmental fate and environmental toxicology of Imazapyr are described in PRVD2008-10 Imazapyr.

Imazapyr will pose negligible risk to earthworms, bees, birds and wild mammals under conditions of field use. The risk to aquatic organisms is also negligible. Imazapyr poses a potential risk to non-target terrestrial plants. This risk can be mitigated by precautionary label statements and the establishment of terrestrial buffer zones for the protection of these habitats.

Value Considerations

What Is the Value of Ares Herbicide ?

Ares Herbicide contains the active ingredients imazapyr at 15 grams and imazamox at 33 grams per litre of product. Ares Herbicide is a post-emergence herbicide which is applied using ground application equipment to Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait) to control broadleaf and grassy weeds. Ares Herbicide provides an alternative to control of annual grassy and broadleaved weeds specifically in Clearfield crops and provides control of wild oat (including Group 1 and Group 8 resistant biotypes), green foxtail (including Group 1 and Group 3 resistant biotypes), volunteer wheat (all varieties except those with the Clearfield trait), volunteer barley, Japanese brome and Persian darnel.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Ares Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with imazapyr on the skin or through inhalation of spray mists, anyone mixing and loading Ares Herbicide must wear a long-sleeved shirt, long pants, chemical-resistant gloves and goggles or a face shield, and anyone applying Ares Herbicide must wear a long-sleeved shirt and long pants. In addition, standard label statements to protect against drift during application were added to the label.

Environment

Key risk-reduction measures for the protection of the environment include precautionary label directions and buffer zones for the new end-use product Ares Herbicide:

- Toxicity statement for non-target terrestrial plants;
- Terrestrial buffer zone of 1 metre for field sprayer application, based on Imazapyr toxicity. However, as Ares Herbicide contains also the active ingredient Imazamox, a terrestrial buffer zone of 11 metres for field sprayer application based on Imazapyr toxicity supersedes the default 1-metre buffer zone for Imazapyr.

Next Steps

Before making a final registration decision on imazapyr, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please note that, to comply with Canada's international trade obligations, consultation on the proposed MRLs will also be conducted internationally via a notification to the World Trade Organization. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency’s response to these comments.

Other Information

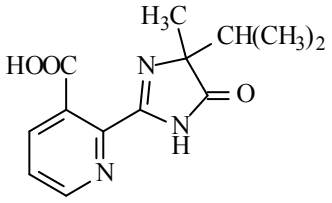
When the PMRA makes its registration decision, it will publish a Registration Decision on imazapyr (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA’s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

Science Evaluation

Imazapyr

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	**Imazapyr**
Function	**Herbicide**
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	**2-(4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl)nicotinic acid**
2. Chemical Abstracts Service (CAS)	**2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-3-pyridinecarboxylic acid**
CAS number	**81334-34-1**
Molecular formula	**$C_{13}H_{15}N_3O_3$**
Molecular weight	**261.3**
Structural formula	
Purity of the active ingredient	98.8%

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

Technical Product—Imazapyr Technical Herbicide

Property	Result
Colour and physical state	White solid
Odour	Slight odour of acetic acid
Melting range	169-173°C
Boiling point or range	Not applicable
Density	1.03-1.08 kg/L
Vapour pressure at 60°C	< 0.013 mPa

Property	Result
Ultraviolet (UV)-visible spectrum	No absorbance at $\lambda > 300$ nm
Solubility in water	9.74 g/L at 15°C 11.3 g/L at 25°C
Solubility in organic solvents at 20°C (g/L)	Solvent — Solubility (g/L) Acetone — 33.9 Dimethyl sulfoxide — 471 Hexane — 0.0095 Methanol — 105 Dichloromethane — 87.2 Toluene — 1.80
n-Octanol-water partition coefficient (K_{ow})	Log K_{ow} = 0.11
Dissociation constant (pK_a)	pK_{a1} = 1.9 pK_{a2} = 3.6 pK_{a3} = 11
Stability (temperature, metal)	Stable for at least 2 years at 25°C, 1 year at 37°C and 3 months at 45°C. There is no reactive chemical hazard associated with exposure to common metals under normal conditions of storage.

End-Use Product—Ares Herbicide

Property	Result
Colour	Pale yellow to amber
Odour	Aliphatic odour
Physical state	Liquid
Formulation type	Solution
Guarantee	Imazapyr……..15 g/L Imazamox……33 g/L
Container material and description	HDPE containers with inner barrier (e.g. Polyamide) and with foil seal; 0.25 - 100 L and bulk.
Density	1.07-1.09 g/cm^3
pH of 1% dispersion in water	6.3
Oxidizing or reducing action	The product does not have any oxidizing properties. No reaction with water or iron. It does react weakly with oxidizing agents.
Storage stability	Stable for 2 years at 28°C stored in high density polyethylene packs.
Corrosion characteristics	No corrosion to packaging material after 4 years storage at 20°C.
Explodability	Expert assessment indicates no evidence of explosive properties.

1.3 Directions for Use

Ares Herbicide is a selective herbicide for use as a post-emergence treatment on Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait) for the control of specific broadleaf and grassy weeds. The product is applied once per growing season, in the spring, as a broadcast treatment with ground application equipment only. Ares Herbicide can be applied at a rate of 29 g a.i./ha (20.0 g a.i./ha imazamox and 9.0 g a.i./ha imazapyr) and must be applied with Merge Adjuvant at a rate of 0.5% v/v (e.g., 5 L of Merge Adjuvant per 1000 L spray solution) (See Table 1.3.1).

Table 1.3.1 Weed Control Claims for Ares Herbicide*

Herbicide Rate	Weeds Controlled	
	Broadleaf Weeds	**Grassy Weeds**
29 g a.i./ha or 0.604 L product/ha (20 g a.i./ha imazamox + 9 g a.i./ha imazapyr)	cleavers, cow cockle, green smartweed, hemp-nettle, lamb's quarters, redroot pigweed, shepherd's purse, stinkweed, wild buckwheat, wild mustard, volunteer tame mustard, volunteer canola (non-Clearfield canola varieties only)	barnyard grass, green foxtail, spring germinating Japanese brome grass, wild oats, yellow foxtail, Persian darnel, volunteer canary seed, volunteer durum wheat, volunteer barley, volunteer tame oats, volunteer spring wheat (non-imazamox tolerant wheat)

* Ares Herbicide must be applied with Merge Adjuvant at a rate of 0.5% v/v (e.g., 5 L of Merge Adjuvant per 1000 L spray solution)

Ares Herbicide may be tank mixed with one of the following 3 tank mix partners to broaden the spectrum of broadleaf and grassy weed control: Lontrel Dry, Lontrel 360, or Equinox EC.
The following restrictions are to be applied:

- For sale for use in the Prairie Provinces and Peace River Region of British Columbia
- Use of Ares Herbicide on canola, canola quality *Brassica juncea* or lentil varieties not designated with the Clearfield trait may cause severe injury.

1.4 Mode of Action

Imazapyr is classified as a Group 2 Herbicide (refer to Regulatory Directive DIR99-06, Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action, for details). The primary mode of action of imazapyr is as an inhibitor of the plant enzyme acetolactate synthase (ALS) in target weeds. ALS is a key enzyme in the synthesis of branched-chain amino acids. The inhibition of the ALS enzyme results in a number of distinctive whole plant symptoms. Growth in sensitive plant species is retarded within hours of application although visible effects may not be observed for several days. Symptoms appear first in the

upper meristematic regions of the plant as chlorosis and necrosis. The upper new leaves often take on a wilted appearance. The effect then spreads to the remaining parts of the plant. Reddening of the midrib and vein is observed in some species. Chlorosis and tissue necrosis may not be apparent in some plant species until two weeks after application. Imazapyr is readily absorbed by plant foliage and roots; imazapyr is mobile in both the xylem and the phloem and accumulates in the primary and auxiliary meristems of the plant.

Imazapyr is one of two Group 2 herbicide active ingredients contained in the end-use product Ares Herbicide. Ares Herbicide contains imazapyr at 15 grams per litre and imazamox at 33 grams per litre of product.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

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

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

Capillary electrophoresis with ultraviolet spectroscopy methods (CE-UV) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

Method M 3519, developed for the determination of imazamox and imazethapyr residues in/on plant commodities, was modified for the determination of imazapyr, a compound of similar chemistry to those analytes already determined by the method. Methods M 3223, M 3075 and M 3184 were developed for the determination of imazapyr in/on milk fat, milk and livestock commodities, respectively. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries were obtained in plant and livestock matrices. Adequate extraction efficiencies were demonstrated using radiolabelled milk and kidney analyzed with Methods M 3075 and M 3184, respectively. Methods M 3519, M 3075 and M 3184 were successfully validated by an independent laboratory.

A weight of evidence rationale was submitted explaining why imazapyr was not evaluated according to the US FDA Multiresidue Methods (MRMs), and why in general the MRM do not work for imidazolinones. It is concluded that these methods would not be adequate to determine residues of imazapyr

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Imazapyr is a herbicide belonging to the imidazolinone chemical class. A detailed review of the toxicological database for imazapyr was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The majority of the studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices (GLP). Some studies were conducted prior to GLP implementation, however they were considered to be of acceptable scientific quality and met the applicable guideline at the time of conduct. Overall, the scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to imazapyr.

Following a single oral radiolabelled dose in rats, imazapyr was rapidly absorbed from the digestive tract, absorption accounting for approximately 71-81% of the administered dose (AD). Urinary (55-91% of the AD) and fecal (3-32% of the AD) excretion was rapid, and the majority occurred within the first 24 hours. The elimination half-life of imazapyr was less than 24 hours in both sexes. The overall recovery of administered radioactivity (urine, feces and carcass) at 168 hours post-dosing in all groups (single low-dose, multiple low-dose and intravenous dose groups) ranged from 92-108% of the AD. Less than 0.2% of the AD was measured in expired air of both sexes. The distribution pattern of radioactivity was similar between sexes. A very low level of radioactivity was retained in tissues and organs. Less than 0.2% of the AD was detected in the residual carcasses and the radioactive residue in tissues and organs accounted for less than 0.01% of the AD. The highest concentrations of radioactivity were found in the kidneys and liver (both sexes). Under the condition of the study, there was no evidence of bioaccumulation in either sex. The parent compound was excreted virtually unchanged via the urine and feces representing 78-96% of the AD. Metabolism occurred via the hydrolytic cleavage of the imidazolinone ring resulting in 2 minor metabolites, CL 252,974 and CL 60,032, that accounted for equal to or less than 0.05% of the AD. The unidentified metabolites (up to 12) represented less than 3% of the AD (0-48 hrs).

Imazapyr was of low acute toxicity by the oral and dermal routes, but was of slight toxicity via the inhalation route. Imazapyr was non-irritating to the skin and was not a dermal sensitizer in guinea pigs (Buehler method). However, it was severely irritating to the eye.

The end-use product, Ares Herbicide, was of low acute toxicity via the oral, dermal and inhalation routes. It was minimally irritating to the eye and slightly irritating to the skin. Ares Herbicide was not a dermal sensitizer in guinea pigs (Buehler method).

Short-term repeated oral dosing with high doses of imazapyr did not result in any adverse effects. Treatment-related increased relative kidney and liver weights in high-dose females in the 90-day rat study, and in mid- and high-dose females in the 12-month dog study, respectively, were not associated with any histopathological findings. Short-term repeated dermal dosing in rabbits produced no evidence of dermal or systemic toxicity up to the highest practical dose.

In the 18-month mouse carcinogenicity study, imazapyr caused no toxicity at any dose tested. The dosing was considered adequate based on the use of a limit dose. There was no evidence of carcinogenic potential in the mouse.

In the 24-month combined chronic/carcinogenicity study in rats, toxicity was limited to early deaths and reduced survivorship noted in high-dose males. There were no signs of toxicity pointing to a consistent cause of death for the early decedents. There was a marginal increased incidence of combined benign/malignant brain astrocytomas observed at the highest dose. These tumors are considered to be uncommon and the incidence at the highest dose was outside the historical control range. However, the highest dose exceeded the maximum tolerated dose (MTD) as evidenced by mortality. Generally, effects noted at doses that exceed the MTD are not considered relevant to the risk assessment.

When imazapyr was tested in a battery of *in vitro* and *in vivo* genotoxicity assays, imazapyr was negative in five assays (reverse mutation assay, dominant lethal assay, unscheduled DNA synthesis assay, chromosomal aberration assay, and micronucleus assay) and equivocal in one assay (gene mutation assay). Overall, there was no concern for genotoxic potential for imazapyr.

Neurotoxicity studies were not conducted as there was no indication of neurotoxicity in the toxicity database.

In the 2-generation reproductive toxicity study, no treatment-related effects were observed in the parental rats and in the offspring. The dosing was considered adequate based on the use of a limit dose. There was no evidence of reproductive toxicity.

There was no evidence of increased susceptibility of the young in the oral rat and rabbit developmental toxicity studies with imazapyr. The maternal rats showed excessive salivation at the highest dose tested likely associated with gavage dosing, while fetuses exhibited no effects. No maternal or developmental toxicity was noted in the rabbit developmental toxicity study.

Overall, imazapyr showed very low mammalian toxicity. There was no indication of target organ toxicity or sex/species sensitivity. There was also no indication of increased toxicity with increased duration of exposure in any tested species.

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

Incident Reports
Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the PMRA website. Incidents from Canada and the United States were searched and reviewed for imazapyr. As of 20 May 2011, five incident reports involving human or domestic animals were submitted for products containing imazapyr. Three and two incidents occurred in Canada and the United States, respectively. In three of the five cases, imazapyr was accompanied by one to two other active ingredients in the product formulations. Only one of the five reports involved human exposure; symptoms included tongue swelling, respiratory irritation, collapsed lung and asthma. There was insufficient information to relate these clinical effects with exposure to imazapyr. The animal reports contained several effects including vomiting, respiratory issues (e.g. edema, distress), tachycardia, weight loss, low milk production, and malaise or death following contact or ingestion. These animal incidents were unlikely to be caused by products containing imazapyr.

In the EPA Re-evaluation Decision Document (2006), the EPA indicated that approximately 20 incidents (documented from various database between 1982-2004) involved human exposure to imazapyr. However, EPA stated that none of these incidents were listed under the "definite", "probable" or "possible" certainty categories. Symptoms most commonly reported included eye irritation, dermal irritation, throat irritation, nausea, and coughing or choking.

The PMRA concluded that the information from the incident reports did not impact the risk assessment. Detailed information for the incidents can be found on the PMRA Public Registry.

3.1.1 PCPA Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects to take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.
With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, extensive data were available for imazapyr. The database contains the full complement of required studies including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, there was no indication of increased susceptibility of fetuses or offspring compared to parental animals in the reproductive and prenatal developmental toxicity studies. There were no developmental effects observed in the rat and rabbit developmental toxicity studies. On the basis of this information, the PCPA factor was reduced to 1-fold.

3.2 Acute Reference Dose (ARfD)

An acute reference dose was not established as there were no acute endpoints of concern.

3.3 Acceptable Daily Intake (ADI)

To estimate dietary risk of repeat exposure, the 24-month rat combined chronic/carcinogenicity study was selected for risk assessment with a NOAEL of 253 mg/kg bw/day. At the LOAEL of 503 mg/kg bw/day, early deaths and reduced survivorship were seen. This was the lowest NOAEL in the database and was relevant for the establishment of the ADI. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability have been applied. As discussed in the PCPA Hazard Consideration section, the PCPA factor was reduced from 10-fold to 1-fold. **The composite assessment factor (CAF) is 100**.

The selection of this study and CAF is considered protective of all populations, including nursing infants and the unborn children of exposed female workers.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{253 \text{ mg/kg bw/day}}{100} = 2.53 \text{ mg/kg bw/day of imazapyr}$$

No cancer risk assessment was required.

3.4 Occupational and Residential Risk Assessment

Ares Herbicide is a co-formulation of imazapyr and imazamox. The use of Ares Herbicide fits within the registered use pattern of imazamox; therefore, it will not be further discussed in the occupational exposure and risk section.

3.4.1 Toxicological Endpoints

Occupational exposure to Ares Herbicide is characterized as short- to intermediate-term and is predominantly by the dermal and inhalation routes.

Short- and Intermediate-term Dermal
There were no toxicological concerns identified in oral toxicity studies that assess endpoints that are not, by virtue of study design, examined in the short-term dermal study. There was no systemic or dermal toxicity at any dose tested in the 21-day dermal study up to the highest practical dose. Therefore, a quantitative approach for dermal risk assessment was not required.

Short- and Intermediate-term Inhalation
For short- and intermediate-term exposure via the inhalation route, the NOAEL of 282 mg/kg bw/day from the 12-month dog study, the lowest no effect level in short-term studies, was selected for risk assessment.

The target Margin of Exposure (MOE) for this scenario is 100, which includes uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. The selection of this study and MOE is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Incidental Oral Ingestion
For incidental oral exposure, the NOAEL of 282 mg/kg bw/day from the 12-month dog study, the lowest no effect level in short-term studies, was selected for risk assessment. The standard uncertainty factors of 10-fold each have been applied to account for intraspecies variability in toxicological responses and interspecies extrapolation. The target MOE is 100.

3.4.1.1 Dermal Absorption

Dermal absorption data were not submitted.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Individuals have potential for exposure to Ares Herbicide during mixing, loading and application. Exposure to workers mixing, loading and applying imazapyr is expected to be short- to intermediate- term in duration and to occur primarily by the dermal and inhalation routes. However, it was concluded in the toxicology assessment that a quantitative approach for dermal risk assessment was not required. As such, a quantitative chemical handler risk assessment was conducted for inhalation exposure only.

Exposure estimates were derived for mixers/loaders/applicators applying imazapyr to Clearfield Canola, Clearfield Lentils, and Clearfield Canola Quality *Brassica Juncea* using groundboom application equipment. The exposure estimates are based on workers wearing a long-sleeved shirt, long pants, chemical-resistant gloves and goggles or face shield when mixing and loading, and a long-sleeved shirt and long pants when applying.

As chemical-specific data for assessing human exposures were not submitted, inhalation exposure estimates for workers were estimated using the Pesticide Handlers Exposure Database (PHED), version 1.1. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data which facilitates the generation of scenario-specific exposure estimates. Data with the highest confidence were used when available.

Inhalation exposure was estimated by coupling the unit exposure values with the amount of product handled per day with 100% inhalation absorption. Exposure was normalized to mg/kg bw/day by using 70 kg adult body weight.

Exposure estimates were compared to the toxicological endpoints (NOAEL; no observed adverse effects levels) to obtain the margin of exposure (MOE); the target MOE is 100.

Mixer/Loader/Applicator Dermal Exposure Estimates and MOE

Exposure scenario	PHED unit exposure (µg/kg ai handled)[a]	ATPD (ha/day) [b]	Rate (kg ai/ha)	Daily exposure (mg/kg bw/day)[c]	MOE[d]
Open mixing/loading and open cab groundboom application PPE: Single layer (+ gloves when mixing/loading) with no respirator					
Farmer	2.56	107	0.00906	3.55E-05	7954176
Custom applicator	2.56	360	0.00906	1.19E-04	2364158

[a] PHED inhalation unit exposure for mixing/loading/applying = 1.60 µg ai/handled (for open mixing/loading liquids) + 0.96 µg/kg ai handled (for open cab groundboom application) = 2.56 µg/kg ai handled
[b] Default Area Treated per day (ATPD)
[c] Daily exposure = (PHED unit exposure x ATPD x Rate) / (70 kg bw x 1000 µg/mg)
[d] Margin of Exposure (MOE) = Daily Exposure / NOAEL
Based on NOAEL = 282 mg/kg bw/day, target MOE = 100 from 12-month dog study

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering areas treated with Ares Herbicide when scouting, irrigating and hand weeding treated crops. Given the nature of activities performed, the duration of exposure is considered to be short- to intermediate-term and the primary route of exposure for workers that enter treated fields would be dermal, through contact with residues on leaves.

However, it was concluded in the toxicology assessment that a quantitative approach for dermal risk assessment was not required. As such, a quantitative postapplication risk assessment was not conducted. Nevertheless, a restricted entry interval (REI) of 12 hours is required, which is the minimum REI for agricultural crops.

3.4.3 Residential Exposure and Risk Assessment

There are no residential uses for Ares Herbicide and as such, as residential risk assessment was not required.

3.4.3.1 Bystander Exposure and Risk

Bystander exposure should be negligible since the potential for drift is expected to be minimal. Application is limited to agricultural crops only when there is low risk of drift to areas of human habitation or activity such as houses, cottages, schools and recreational areas, taking into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

As the use of imazamox fits within the registered use pattern for this active on Clearfield canola, Clearfield canola quality *Brassica juncea* and Clearfield lentils, exposure to residues of imazamox in food and drinking water is not anticipated to change. Residue chemistry for imazamox will not be further discussed in the present document.

The residue definition for risk assessment and enforcement in plant commodities (cereals, pulses and oilseeds) is imazapyr. The data gathering/enforcement analytical method M 3519 is valid for the quantification of imazapyr residues in/on plant commodities. The residues of imazapyr are stable in corn grain, forage and fodder when stored in a freezer for up to 27 months. The corn freezer storage stability data could not be extrapolated to support the storage intervals of the canola and lentil seed samples and processed commodities (canola meal and oil). This is because the freezer storage stability data for corn grain (high starch content) cannot be extended to lentil seed (high protein content) or to canola seed and the processed commodities (high oil content). When treated canola seed was processed, residues of imazapyr concentrated in canola meal, but not in refined oil. Supervised residue trials conducted in Canada using end-use products containing imazapyr at approximately the label rate in canola and lentils are sufficient to support the proposed maximum residue limits.

The residue definition for risk assessment and enforcement in livestock commodities is imazapyr. The data gathering analytical methods M 3223, M 3075 and M 3184 are valid for the quantitation of imazapyr in/on milk fat, milk and tissues, respectively. Methods M 3075 and M 3184 are valid for the enforcement of imazapyr residues in/on milk and tissues, respectively. Finite residues of imazapyr are not anticipated in/on livestock commodities from the proposed uses on Clearfield canola, Clearfield canola quality *Brassica juncea* and Clearfield lentils.

3.5.2 Dietary Risk Assessment

A chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The basic chronic dietary exposures from all supported imazapyr food uses (alone) for the total population, including infants and children, and all representative population subgroups are 0.00% of the acceptable daily intake (ADI). Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to imazapyr from food and water is 0.00% (0.000466 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1-2 years old at 0.00% (0.001091 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

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

3.5.3 Aggregate Exposure and Risk

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

3.5.4 Maximum Residue Limits

Proposed Maximum Residue Limits

Commodity	Recommended MRL (ppm)
Dry lentils	0.2
Eggs; fat, meat, and meat byproducts of cattle, goats, hogs, horses, poultry and sheep; rapeseed subgroup (Crop Subgroup 20A)	0.05
Milk	0.01

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

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

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and the chronic dietary risk estimates are summarized in Tables 5, 6 and 7 in Appendix I.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

The environmental fate of imazapyr is described in PRVD2008-10 *Imazapyr*. Overall, imazapyr is stable to hydrolysis, soil photolysis, and biotransformation in soil and water. But it was found to degrade rapidly by water photolysis. It is unlikely to bioaccumulate.

Imazapyr was reported to have the potential to be mobile in the environment. However, modelling results from the USEPA generally predicted low concentrations in ground and surface water, and conclusions are that exposure from groundwater and surface water are expected to be minimal and not of concern.

4.2 Environmental Risk Characterization

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

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

An environmental assessment was conducted on Imazapyr Technical herbicide for the formulation of Ares Herbicide for use in agricultural fields on specific Clearfield tolerant plants. The proposed new use (USC 14: terrestrial food crops) is not expected to result in significant exposure of non-target organisms in the environment to the active ingredient Imazapyr. The risk to non-target organisms is considered to be negligible if used according to the product label.

4.2.1 Risks to Terrestrial Organisms

Under the proposed new use (terrestrial food crops), the following new terrestrial toxicity data were submitted:

- one earthworm species (acute exposure), one species of honeybee (oral and contact exposure), using an Imazamox-Imazapyr formulation as the test substance;
- two bird species representing vertebrates (reproduction, representing long-term exposure), using Imazapyr only as the test substance.

The resulting toxicity endpoints are presented in Appendix I, Table 8.

Risk to terrestrial organisms was based upon the newly submitted data, as well as the existing PMRA toxicity data and the data used for the re-evaluation of Imazapyr. Ares Herbicide is not expected to adversely affect terrestrial invertebrates, or birds and mammals, under the proposed use expansion (Appendix I, Tables 9 and 10).

A risk was identified at the screening level (RQs > 1) for terrestrial plants. But when a refinement with a 6% spray drift at 1 metre off field was applied, the risk quotients were lower than the value of 1 (Appendix I, Table 9), suggesting that the vegetation should not be impacted by imazapyr spray drift beyond 1 metre. Therefore a default buffer zone of 1 metre is sufficient to protect non-target terrestrial plants.

4.2.2 Risks to Aquatic Organisms

Under the proposed new use (terrestrial food crops), the following new aquatic toxicity data using an Imazamox-Imazapyr formulation as the test substance were submitted: one freshwater aquatic invertebrate (acute exposure), one freshwater fish (acute exposure), and one freshwater algal species (acute exposure). The resulting toxicity endpoints are presented in Appendix I, Table 8.

Risk to aquatic organisms was based upon the newly submitted data, as well as the existing PMRA toxicity data and the data used for the re-evaluation of imazapyr. Overall, the risk assessment indicates that Ares Herbicide is not expected to adversely affect freshwater or marine invertebrates, fish, or algae under the proposed use expansion. Toxicity values in Table 11 are normalized for an LOC of 1 by multiplying either a factor of 0.5 or 0.1 (Appendix I, Table 11).

5.0 Value

5.1 Effectiveness Against Pests

5.1.1 Ares Herbicide

Data from 38 replicated field trials conducted over a 2-year period (2008 and 2009) at several locations in 3 provinces (Alberta, Saskatchewan and Manitoba) were submitted. For each trial, an appropriate experimental design was used, and an appropriate set of treatments was used to address the proposed pest claims. Treatments also included various rates of Ares Herbicide to determine the lowest effective rate. In general, the herbicide treatments were applied within the proposed growth range for the broadleaf and grass weeds using small plot application equipment.

The efficacy of Ares Herbicide applied as a stand-alone herbicide treatment or in tank mixtures with other herbicides for control of individual weed species was visually assessed as percent weed control and compared to an untreated weedy check. Observations were made up to three times throughout the growing season.

5.1.2 Acceptable Efficacy Claims for Ares Herbicide

The submitted efficacy data established the lowest effective rate for the Ares Herbicide treatment applied alone and support the weed control claims that are summarized in Table 5.1.2.1. Ares Herbicide must be applied with Merge Adjuvant.

Table 5.1.2.1 Weed Control Claims for Ares Herbicide*

Herbicide Rate	Weeds Controlled	
	Broadleaf Weeds	Grassy Weeds
29 g a.i./ha or 0.604 L product/ha (20 g a.i./ha imazamox + 9 g a.i./ha imazapyr)	cleavers, cow cockle, green smartweed, hemp-nettle, lamb's quarters, redroot pigweed, shepherd's purse, stinkweed, wild buckwheat, wild mustard, volunteer tame mustard, volunteer canola (non-Clearfield canola varieties only)	barnyard grass, green foxtail, spring germinating Japanese brome grass, wild oats, yellow foxtail, Persian darnel, volunteer canary seed, volunteer durum wheat, volunteer barley, volunteer tame oats, volunteer spring wheat (non-imazamox tolerant wheat)

* Ares Herbicide must be applied with Merge Adjuvant at a rate of 0.5% v/v (e.g., 5 L of Merge Adjuvant per 1000 L spray solution)

5.1.3 Herbicide Tank Mix Combinations

Adequate data were submitted to support the weed control claims for the proposed herbicide tank mixture of Ares Herbicide with each of the following tank mix partners: Lontrel Dry or Lontrel 360 (Table 5.1.3.1), or Equinox EC (Table 5.1.3.2). No reduction in weed control was observed when Ares Herbicide was tank mixed with any of the tank mix partners.

Table 5.1.3.1 Weed Control Claims for Ares Herbicide in Tank Mix With Lontrel Dry or Lontrel 360

Product	Rate (g a.i./ha)	Weeds Controlled	
		Broadleaf Weeds	Grassy Weeds
Ares Herbicide*	29 (20 g a.i./ha imazamox + 9 g a.i./ha imazapyr)	cleavers, cow cockle, green smartweed, hemp-nettle, lamb's quarters, redroot pigweed, shepherd's purse, stinkweed, wild buckwheat, wild mustard, volunteer tame mustard, volunteer canola (non-Clearfield canola varieties only), season-long top-growth control of perennial and annual sow thistle and Canada thistle	barnyard grass, green foxtail, spring germinating Japanese brome grass, wild oats, yellow foxtail, Persian darnel, volunteer canary seed, volunteer durum wheat, volunteer barley, volunteer tame oats, volunteer spring wheat (non-imazamox tolerant wheat)
Lontrel Dry or Lontrel 360	75		

* Ares Herbicide must be applied with Merge Adjuvant at a rate of 0.5% v/v (e.g., 5 L of Merge Adjuvant per 1000 L spray solution)

Table 5.1.3.2 Weed Control Claims for Ares Herbicide in Tank Mix With Equinox EC

Product	Rate (g a.i./ha)	Weeds Controlled	
		Broadleaf Weeds	Grassy Weeds
Ares Herbicide*	29 (20 g a.i./ha imazamox + 9 g a.i./ha imazapyr)	cleavers, cow cockle, green smartweed, hemp-nettle, lamb's quarters, redroot pigweed, shepherd's purse, stinkweed, wild buckwheat, wild mustard, volunteer tame mustard, volunteer canola (non-Clearfield canola varieties only)	barnyard grass, green foxtail, spring germinating Japanese brome grass, wild oats, yellow foxtail, Persian darnel, volunteer canary seed, volunteer durum wheat, volunteer barley, volunteer tame oats, volunteer spring wheat (non-imazamox tolerant wheat), plus grass species listed on the Equinox EC label
Equinox EC	26.7-50**		

* Ares Herbicide must be applied with Merge Adjuvant at a rate of 0.5% v/v (e.g., 5 L of Merge Adjuvant per 1000 L spray solution)

** The higher rate of Equinox EC should be used when weed staging is late, or when weeds are under stress and not growing as actively due to moisture stress or temperature stress.

5.2 Phytotoxicity to Host Plants

Data from 25 replicated field trials [12 trials in Clearfield canola (e.g., canola varieties with the Clearfield trait), 12 trials in Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and 11 trials in Clearfield lentils (e.g., lentil varieties with the Clearfield trait)] conducted over a 2-year period (2008 and 2009) at several locations in 3 provinces (Alberta, Saskatchewan and Manitoba) were submitted. For each trial, an appropriate experimental design was used, and an appropriate set of treatments was used to address the proposed host plant claims.

Crop injury (%) was visually assessed up to three times during the growing season. Crop yield, expressed as a percentage of a weed-free check, was reported in all trials.

5.2.1 Acceptable Claims for Host Plants

Crop injury data with Ares Herbicide applied alone or in tank-mixture support a crop tolerance claim for Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait) when viewed in conjunction with the crop yield data (Table 5.2.1.1).

Table 5.2.1.1 Crop Claims for Ares Herbicide and in Tank Mix with Lontrel Dry, Lontrel 360 or Equinox EC

Treatment	Rate (g a.i./ha)	Crop
Ares Herbicide*	29 (20 g a.i./ha imazamox + 9 g a.i./ha imazapyr)	Clearfield canola Clearfield canola quality *Brassica juncea* Clearfield lentils
Ares Herbicide* + Lontrel Dry or Lontrel 360	29 + 75	Clearfield canola
Ares Herbicide* + Equinox EC	29 + (26.7-40)**	Clearfield canola Clearfield canola quality *Brassica juncea*
	29 + (26.7-50)**	Clearfield lentils

* Ares Herbicide must be applied with Merge Adjuvant at a rate of 0.5% v/v (e.g., 5 L of Merge Adjuvant per 1000 L spray solution)

** The higher rate of Equinox EC should be used when weed staging is late, or when weeds are under stress and not growing as actively due to moisture stress or temperature stress.

Use of Ares Herbicide on canola, canola quality *Brassica juncea* or lentil varieties not designated with the Clearfield trait may cause severe injury.

5.3 Impact on succeeding Crops

Information to support the rotational crop claims included rationales and data from 7 replicated field trials that were initiated within one year following an application of Ares Herbicide. The number of trials, in which tolerance was evaluated, varied by rotational crop. Some trials included multiple crops. Trials were conducted at several locations in 3 provinces (Alberta, Saskatchewan and Manitoba).

5.3.1 Acceptable Claims for Rotational Crops for imazapyr

The submitted rationales, crop injury and yield data support a rotational crop tolerance claim for the following crops planted one year or two years after application of Ares Herbicide (Table 5.3.1.1).

Table 5.3.1.1 Rotational Crop Claims for Ares Herbicide

One Year After Application	Two Years After Application
Canary seed Chickpeas Durum wheat Field peas Field corn Clearfield canola Clearfield canola quality *Brassica juncea* Lentils including Clearfield lentils Spring wheat including Clearfield spring wheat Spring barley Tame oats	Canola Flax Sunflower

5.4 Economics

Ares Herbicide provides post-emergent control of a broad spectrum of economically important annual grasses and broadleaved weeds in crops with the Clearfield trait (including Clearfield canola, Clearfield canola quality *Brassica juncea* and Clearifeld lentils). Ares Herbicide also provides growers with another tool to enhance the level and consistency of weed control beyond that provided by presently registered herbicides in these crops. The tank mix combinations with Lontrel and Equinox EC provides a multiple mode of action tank mix option to help prevent or delay the onset of weed resistance. Optimal annual grassy and broadleaved weed control is critical to maintain maximum yield of all crops. Providing optimal control of annual weeds as early as possible may also minimize the time and fuel costs required by avoiding the need to apply an additional herbicide for weed escapes and when harvesting the crop in the fall.

5.5 Sustainability

5.5.1 Survey of Alternatives

Current herbicides registered to control annual grassy and broadleaved weeds specifically in Clearfield crops include both Odyssey 70 WDG and Solo 70 WDG herbicides. These herbicides control a wide range of annual weeds in these crops, although weed control may be reduced under adverse conditions such as cool temperatures and increased weed staging.

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Ares Herbicde is a post-emergence herbicide that offers an additional tool for reduced and conventional tillage production systems and provides growers with the flexibility to choose from an array of integrated pest management strategies.

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

Repeated use of herbicides having the same mode of action in a weed control program increases the probability of naturally selecting the biotypes, a group of plants within a species which has biological traits that are not common to the population as a whole, with less susceptibility to the herbicides using that mode of action. Therefore, Ares Herbicide should be tank-mixed with a herbicide with a different mode of action or be used in rotation with herbicides having different modes of action. Ares Herbicide can be tank-mixed with clopyralid (Group 4) and tepraloxydim (Group 1). These tank mix partners would expand the weed spectrum claim.

The Ares Herbicide label includes the resistance management statements, as per Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

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

During the re-evaluation process, Imazapyr and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The details of that evaluation are described in PRVD2008-10, *Imazapyr*. This active ingredient and its transformation products do not meet Track 1 criteria.

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

6.2. Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[6]. The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusion:

- Technical grade Imazapyr and the end-use product Ares Herbicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*

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

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for imazapyr is adequate to define the majority of toxic effects that may result from exposure. There were no effects in the young in reproduction or developmental toxicity studies. Imazapyr is not considered to be a neurotoxicant. There was no evidence of carcinogenicity in mice. Tumors seen in rats were not considered relevant to human risk assessment. In short-term and chronic studies on laboratory animals, there was no indication of target organ toxicity. The only effects observed were early deaths and reduced survivorship in high-dose male rats from the 24-month rat study. The risk assessment protects against the toxic effects noted above by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

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

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

8 DIR2006-02, PMRA Formulants Policy.

9 DIR2006-02, PMRA Formulants Policy.

Mixers/loaders/applicators handling Ares Herbicide and workers re-entering treated fields are not expected to be exposed to levels of imazapyr that will result in an unacceptable risk when Ares Herbicide is used according to label directions. The personal protective equipment on the product label is adequate to protect workers.

The nature of the residue in plants and animals is adequately understood. The residue definition (RD) is imazapyr in all crops (primary and rotational) and livestock commodities. The proposed use of imazapyr on Clearfield canola, Clearfield canola quality *Brassica juncea* and Clearfield lentils 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 for imazapyr:

Commodity	Recommended MRL (ppm)
Dry lentils	0.2
Eggs; fat, meat, and meat byproducts of cattle, goats, hogs, horses, poultry and sheep; rapeseed subgroup (Crop Subgroup 20A)	0.05
Milk	0.01

7.2 Environmental Risk

The proposed new use for imazapyr on terrestrial food crops is not expected to result in significant exposure of non-target organisms in the environment. The risk to non-target organisms is considered to be negligible if used according to the product label.

7.3 Value

The data submitted to register Ares Herbicide are adequate to describe its efficacy for use as a post-emergence application in Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait) to control broadleaf and grassy weeds. Ares Herbicide provides an alternative for the control of annual grassy and broadleaved weeds specifically in Clearfield crops and provides control of wild oat (including Group 1 and Group 8 resistant biotypes), green foxtail (including Group 1 and Group 3 resistant biotypes), volunteer wheat (all varieties except those with the Clearfield trait), volunteer barley, Japanese brome and Persian darnel.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Imazapyr Technical Herbicide and Ares Herbicide, containing the technical grade active ingredient imazapyr, to control broadleaf and grassy weeds in Clearfield canola (e.g., canola varieties with the Clearfield trait), Clearfield canola quality *Brassica juncea* (e.g., canola quality *Brassica juncea* varieties with the Clearfield trait), and Clearfield lentils (e.g., lentil varieties with the Clearfield trait).

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

List of Abbreviations

VSAD

a.i.	active ingredient
g	gram
ha	hectare(s)
L	litre
v/v	volume per volume dilution

CES

CE-UV	capillary electrophoresis-ultraviolet spectroscopy
CL 9140	2,3-pyridinedicarboxylic acid
CL 119060	7-hydroxyfuro[3,4-b]pyridine-5(7H)-one
LOQ	limit of quantitation

FREAS

a.i.	active ingredient
a.e.	acid equivalents
ADI	acceptable daily intake
CE	Capillary electrophoresis
bw	body weight
DAT	Days after treatment
EEC	estimated environmental concentration
g	gram
ha	hectare(s)
kg	kilogram
LC-MS	Liquid chromatography with mass spectrometry
LC-MS/MS	Liquid chromatography with tandem mass spectrometry
LOQ	limit of quantitation
mg	milligram
MRL	maximum residue limit
PHI	preharvest interval
ppm	parts per million
RAC	raw agricultural commodity
TRR	total radioactive residues
FDA MRM	U.S. Food and Drug Administration Multiresidue Methods
µg	micrograms

OEAS

ATPD	area treated per day
MOE	margin of exposure
NOAEL	no observable adverse effect level
PHED	Pesticide Handlers Exposure Database
REI	restricted entry interval

EAD	
μg	micrograms
a.i.	active ingredient
BW	body weight
dw	dry weight
DT_{50}	dissipation time of 50% of the test substance
EC_{25}	effective concentration on 25% of the population
EDE	estimated daily exposure
EEC	estimated environmental exposure concentration
EP	end-use product
FC	food consumption
FIR	food ingestion rate
g	gram
ha	hectare(s)
kg	kilogram
K_{ow}	octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOEC	lowest observed effect concentration
mg	milligram
mL	millilitre
NOEC	no observed effect concentration
NOEL	no observed effect level
PMRA	Pest Management Regulatory Agency
$t_{1/2}$	half-life
TGAI	Technical grade active ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency

TOX	
AD	administered dose
ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
bw	body weight
CAF	composite assessment factor
g	gram(s)
GLP	good laboratory practices
hr(s)	hour(s)
iv	intravenous
kg	kilogram(s)
L	litre(s)
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
mg	milligram(s)

MAS	maximum average score for 24, 48 and 72 hours
MIS	maximum irritation score
MOE	margin of exposure
MOLD	multiple oral low dose
MTD	maximum tolerated dose
NOAEL	no observed adverse effect level
NZW	New Zealand White
PCPA	*Pest Control Product Act*
PMRA	Pest Management Regulatory Agency
ppm	parts per million
rel	relative
SOHD	single oral high dose
SOLD	single oral low dose
TGAI	technical grade active ingredient

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Soil	M 3014	Imazapyr	CE-UV	1.0 ppb	1888203
Sediment	The method used for soil was extended to sediment.				
Water	M 3001	Imazapyr	CE-UV	1.0 ppb	1888204
	M 3097	CL 9140	CE-UV	2.0 ppb	1888205
	M 3097	CL 119060	CE-UV	2.0 ppb	1888205
Plant	M 3519	Imazapyr (BAS 685 H)	LC-MS (quantitation); LC-MS/MS (quantitation and confirmation) (data gathering and enforcement)	0.05 ppm	921920 796066 1843005 1843006
Animal	M 3223 (milk fat)	Imazapyr	Capillary electrophoresis (CE); LC-MS (confirmation) (data gathering)	0.01	1843009 1843030
	M 3075 (milk)	Imazapyr	Capillary electrophoresis (CE); LC-MS (confirmation) (data gathering and enforcement)	0.01	1843003 1843007 1843010 1843011 1843030
	M 3184 (muscle, liver, kidney and fat)	Imazapyr	Capillary electrophoresis (CE); LC-MS (confirmation) (data gathering and enforcement)	0.05	PMRA # 1843003, 1843008, 1843030

Table 2 Toxicity Profile of End-use Product(s)-Ares Containing Imazapyr
(Effects are known or assumed to occur in both sexes unless otherwise noted; in such case, sex-specific effects are separated by semi-colons)

Study Type/Animal/PMRA #	Study Results
Acute Oral Standard test (401) Sprague-Dawley rats PMRA # 1842969	**Low Toxicity** LD_{50} > 5000 mg/kg bw
Acute Dermal Sprague-Dawley rats PMRA # 1842971	**Low Toxicity** LD_{50} > 5000 mg/kg bw
Acute Inhalation (Nose-only) Sprague-Dawley rats PMRA # 1842973	**Low Toxicity** LC_{50} > 6.18 mg/L Clinical signs: chromodacryorrhea, red nasal discharge, dried red material in facial area and excessive salivation; signs resolved within 2 days
Primary Eye Irritation NZW rabbits PMRA # 1842977	**Minimally irritating to the eye** MAS = 0.89/110 MIS (24 hrs) = 2.67/110
Primary Dermal Irritation NZW rabbits PMRA # 1842975	**Slightly irritating to the skin** MAS = 0.67/8 MIS (24 hrs) = 1.33/110
Skin Sensitization (Buehler method) Dunkin Hartley guinea pigs PMRA # 1842979	**Not a dermal sensitizer**

Table 3 Toxicity Profile of Technical Imazapyr

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such case, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted)

Study Type/Animal/PMRA #	Study Results
RAT (PMRA # 1168383 and # 1858909) The metabolism of imazapyr (CL 243,997) was investigated in groups of 5 to 12 male and/or female Sprague-Dawley rats following gavage administration of [Pyridine ring 6-^{14}C] CL 243,997 or [Carboxylic acid-^{14}C] CL 243,997. **Dosing**: Single oral low dose (SOLD) = 4.4 or 10 mg/kg bw. Single oral high dose (SOHD) = 1000 mg/kg bw. Multiple oral low dose (MOLD) = 10 mg/kg bw/day for 14 days + 1 dose of radiolabelled imazapyr. Intravenous dose (iv) = 10 mg/kg bw. Vehicle: corn oil (except 0.9% saline solution for iv group) **Rate and extent of absorption and excretion**: Imazapyr was rapidly absorbed from the digestive tract. Based on the iv group, 71.4-80.6% of the administered dose (AD) was absorbed in the SOLD and MOLD groups. The predominant route of elimination was urinary and accounted for 58.8-94.6% of the AD following 168 hours post-dosing in all test groups, whereas fecal excretion accounted for 5.5-36.3% of the AD. Urinary (55.3-90.6% of the AD) and fecal (3.0-31.9% of the AD) excretion was rapid and occurred within the first 24 hours. The elimination half-life of imazapyr was less than 24 hours in both sexes. The overall recovery of administered radioactivity (urine, feces and carcass) at 168 hours post-dosing in all groups ranged from 92.1-107.7% of the AD. Only 0.06-0.12% of the AD was measured in expired air of both sexes. **Distribution / target organs (s)**: The distribution pattern of radioactivity was similar between sexes. A very low level of radioactivity was retained in tissues and organs. Less than 0.2% of the AD was detected in the residual carcasses and the radioactive residue in tissues and organs accounted for < 0.01% of the AD. The highest concentrations of radioactivity were found in the kidneys and liver of the SOHD groups (both sexes). In the MOLD groups, radioactivity in the ovaries was detected at 0.031 ppm, whereas in the other treatment groups, the radioactivity was below the limit of detection. Under the condition of the study, there was no evidence of bioaccumulation in either sex. **Toxicologically significant compound(s)**: The parent compound was detected in urine and feces representing 78.3-96.0% of the AD in all test groups. Metabolism occurred via the hydrolytic cleavage of the imidazolinone ring resulting in 2 minor metabolites, CL 252,974 and CL 60,032, that accounted for ≤ 0.05% of the AD. The unidentified metabolites (up to 12) represented < 3.0% of the AD (0-48 hours). The total amount of excreted parent compound and identified metabolites (urine and feces) accounted for 60.3-90.4% of the AD and 2.7-22.9% of the AD, respectively.	

Study Type/Animal/PMRA #	Study Results
Acute Oral Standard test (401) CHRCD rats PMRA # 1978219	**Low Toxicity** LD_{50} > 5000 mg/kg bw
Acute Oral Standard test (401) Sprague-Dawley rats PMRA # 1234165	**Low Toxicity** LD_{50} > 5000 mg/kg bw
Acute Dermal NZW rabbits PMRA # 1978219	**Low Toxicity** LD_{50} > 2000 mg/kg bw
Acute Dermal NZW rabbits PMRA # 1234166	**Low Toxicity** LD_{50} > 2000 mg/kg bw
Acute Inhalation (Whole-body) Sprague-Dawley rats PMRA # 1168413	**Slight Toxicity** LC_{50} > 1.3 mg/L
Primary Eye Irritation NZW rabbits PMRA # 1978219	**Moderately irritating to the eye*** MAS (24, 48 and 72 hrs) = 37/110 MIS (24 hrs) = 22/110 *Not used for labelling purpose.
Primary Eye Irritation NZW rabbits PMRA # 1234167	**Severely irritating to the eye** MAS = 26.2/110 with irritation irreversible within 21 days in 2 animals MIS (24 hrs) = 31.3/110

Study Type/Animal/PMRA #	Study Results
Primary Skin Irritation NZW rabbits PMRA # 1978219	**Minimally irritating to the skin** MAS = 0.083/8 MIS (24 hrs) = 0.33/8
Primary Skin Irritation NZW rabbits PMRA # 1234168	**Non-irritating to the skin** MAS = 0/8 MIS (1 hr) = 0.2/8
Skin Sensitization (Buehler method) Guinea pigs PMRA # 1168374	**Not a dermal sensitizer**
90-Day Oral Toxicity (diet) Sprague-Dawley rats PMRA # 1915661	NOAEL = 815.8/940.4 mg/kg bw/day **815.8/940.4 mg/kg bw/day:** ↑ rel kidney weight (♀, non-adverse)
12-Month Oral Toxicity (diet) Beagle dogs Non-guideline PMRA # 1858861	NOAEL = 282.1/293.7 mg/kg bw/day **≥141.2/138.5 mg/kg bw/day:** ↑ mean band cell count at week 6 and month 3 (♀, non-adverse), ↑ rel liver weight (♀, non-adverse) * Spleen, adrenal gland, epididymis, uterus and pituitary gland were not weighed.
21-Day Dermal Toxicity NZW rabbits PMRA # 1858864	NOAEL (systemic) = 400 mg/kg bw/day NOAEL (dermal irritation) = 400 mg/kg bw/day

Study Type/Animal/PMRA #	Study Results
18-Month Oral Toxicity and Oncogenicity (diet) CD-1 mice PMRA # 1230476, # 1230477, # 1230478	NOAEL = 1855/2394 mg/kg bw/day **No evidence of carcinogenicity**
24-Month Oral Toxicity and Oncogenicity (diet) Sprague-Dawley rats PMRA # 1226045, # 1226355, # 1226356 Study conducted from 1984 to 1986	NOAEL = 252.6/317.6 mg/kg bw/day **503.0/638.6 mg/kg bw/day:** ↓ time to death (♂), ↓ % survivorship (♂) **Tumors:** benign and malignant brain astrocytomas (♂) **Tumors at a dose exceeding MTD**
2-Generation Dietary Reproductive Toxicity Sprague-Dawley rats PMRA # 1226041	*Parental Toxicity* NOAEL = 738.0/933.3 mg/kg bw/day *Offspring Toxicity* NOAEL = 933.3 mg/kg bw/day *Reproductive Toxicity* NOAEL = 738.0/933.3 mg/kg bw/day **No sensitivity of the young**
Oral Developmental Toxicity (gavage) CD albino rats PMRA # 1168378	Supplementary **≥ 250 mg/kg bw/day:** ↑ salivation with ↑ severity
Oral Developmental Toxicity (gavage) CD albino rats PMRA # 1915646	*Maternal Toxicity* NOAEL = 1000 mg/kg bw/day **1000 mg/kg bw/day:** ↑ salivation (non-adverse) *Developmental Toxicity* NOAEL = 1000 mg/kg bw/day **No sensitivity of the young**

Study Type/Animal/PMRA #	Study Results
Oral Developmental Toxicity (gavage) NZW rabbits PMRA # 1168380	Supplementary **≥ 1000 mg/kg bw/day**: ↑ mortality due to erosive gastric lesions
Oral Developmental Toxicity (gavage) NZW rabbits PMRA # 1915648	*Maternal Toxicity* NOAEL = 400 mg/kg bw/day *Developmental Toxicity* NOAEL = 400 mg/kg bw/day **No sensitivity of the young**
Gene mutations in bacteria PMRA # 1915653	**Negative** Tested up to a limit concentration.
Dominant Lethal (gavage) CD albino rats PMRA # 1231736	**Negative** Tested up to a limit dose.
Unscheduled DNA synthesis PMRA # 1231737	**Negative** Tested up to limit and insoluble concentrations.
Chromosome aberrations *in vitro* PMRA # 1231738	**Negative** Tested up to a limit concentration.
Gene mutations in mammalian cells *in vitro* Non-guideline PMRA # 1231739	**Equivocal** - Sporadic, but significant increase in mutant frequency noted in 2 of the triplicates at 250 µg/mL and at 2500 µg/mL with S9, and in 1 of the triplicates at 1000 µg/mL with S9 (↑ ~5-10X compared to solvent control). - There was no dose-response. - Unclear methodology. Tested up to limit and cytotoxic concentrations.

Study Type/Animal/PMRA #	Study Results
Micronucleus assay *in vivo* (gavage) Crl:NMRI mice PMRA # 1858906	**Negative** Tested up to a limit dose.
Acute oral (gavage) Beagle dogs PMRA # 1858862	**Low Toxicity** LD_{50} > 5000 mg/kg bw Clinical sign: emesis, resolved within 24 hrs

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

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary	Not selected.		
	ARfD = Not established as there were no acute endpoints of concern.		
Repeated dietary	24-month rat combined chronic/carcinogenicity study	NOAEL = 253 mg/kg bw/day; based on early deaths and reduced survivorship in males at the LOAEL of 503 mg/kg bw/day	100
	ADI = 2.53 mg/kg bw/day		
Short-term and intermediate-term dermal	Quantitative risk assessment is not required.		
Short-term and intermediate-term inhalation[2]	12-month dog study	NOAEL = 282 mg/kg bw/day (HDT)	100
Non-dietary oral ingestion (short-term)	12-month dog study	NOAEL = 282 mg/kg bw/day (HDT)	100
Cancer	Cancer risk assessment is not required.		

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

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

Table 5 Residue Summary

NATURE OF THE RESIDUE IN IMIDAZOLINONE-RESISTANT CORN			PMRA # 1858920, 1858925	
Radiolabel Position	[pyridine-6-^{14}C]-imazapyr			
Test Site	The study was conducted under field conditions. Two treatment plots and one control plot were established at the test site. Corn seeds were planted in sandy loam soil.			
Treatment	The single broadcast foliar application was made 18 days after planting of the corn seed. The control plot was treated with a mixture of formulation blank and surfactant.			
Rate	A single application at 28 g a.e./ha or 80 g a.e./ha			
End-use product	Imazapyr was formulated with water and non-ionic spreader, and applied as an aqueous ammonium salt solution.			
Preharvest interval (PHI)	Whole corn plants were harvested from each plot at two hours after treatment, and at 14, 30 and 62 days after treatment (0-, 14-, 30- and 62-DAT). At crop maturity (114-DAT), mature corn ears and fodder samples were harvested.			
Rate		**28 g a.e./ha**	**80 kg a.e./ha**	
Matrix	**PHI**	**TRRs (ppm)***	**TRRs (ppm)***	
Green Plant	0-DAT	2.471	8.711**	
Green Plant	14-DAT	0.058	0.153	
Early Forage	30-DAT	0.010***	0.026	
Late Forage	62-DAT	0.004**	0.025	
Mature Fodder	114-DAT	0.009**	0.028	
Mature Grain	114-DAT	0.029	0.086	
*Expressed as imazapyr equivalents. **These samples were not further analyzed. ***Samples of early forage were extracted, but were not further analyzed.				
	28 g a.e./ha		**80 kg a.e./ha**	
Metabolites Identified	**Major Metabolites (>10%TRR)**	**Minor Metabolites (<10% TRR)**	**Major Metabolites (>10%TRR)**	**Minor Metabolites (<10% TRR)**
Green Plant 0-DAT	Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045	Not analyzed	
Green Plant 14-DAT	Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045	Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045

Early Forage 30-DAT	Not analyzed		Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045
Late Forage 62-DAT	Not analyzed		Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045
Mature Fodder 114-DAT	Not analyzed		Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045
Mature Grain 114-DAT	Imazapyr	CL 9,140, CL 60,032; CL 263,078; CL 252,974; CL 252,663; CL 271,045	Imazapyr	CL 9,140, CL 263,078; CL 252,974; CL 252,663; CL 271,045

[Pyridine-6-^{14}C]-imazapyr was slowly metabolized in imidazolinone-resistant corn. The majority of the applied radioactivity remained as unchanged imazapyr in the green plant, forage, fodder and grain samples.

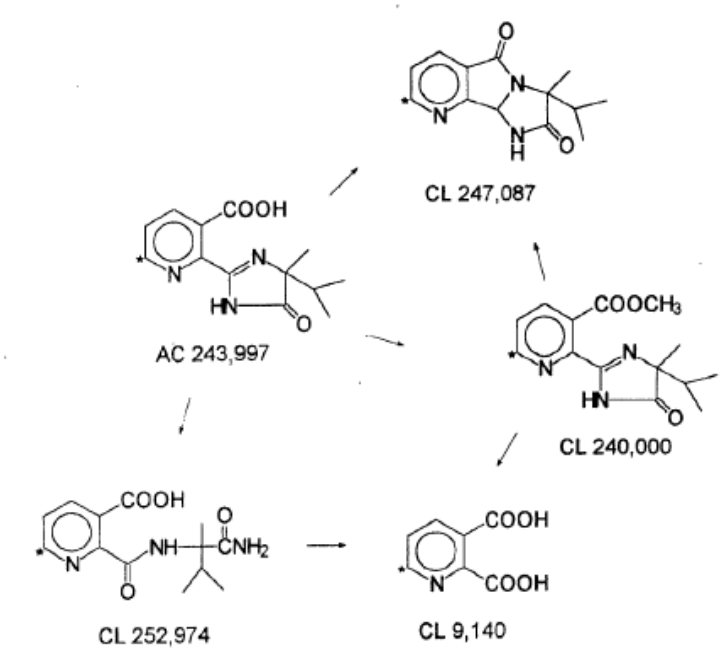
NATURE OF THE RESIDUE IN STRAWBERRY CLOVER	**PMRA # 1858931**
Radiolabel Position	[pyridine-6-^{14}C]-imazapyr
Test Site	The study was conducted under field conditions. Two plots (one control and one treated) were established at the test site. Clover was sown in sandy loam soil.
Treatment	The single broadcast foliar spray application was made to established clover at 69 days after sowing. The control plot was treated with the blank formulation (mixture of isopropylamine, glacial acetic acid and surfactant).
Rate	A single application at 1.68 kg a.e./ha
End-use product	Imazapyr was formulated as an isopropylamine salt in an aqueous solution. The concentrated mixture was diluted with water prior to application.
Preharvest interval (PHI)	Samples of foliage were harvested 0-, 4-, 10-, 15- and 21-DAT.

Matrix	**PHI**	TRRs (imazapyr equivalents)
Clover Foliage	0-DAT	43.006
	4-DAT	37.354
	10-DAT	23.439
	15-DAT	41.617
	21-DAT	49.211

Metabolites Identified	Major Metabolites (>10% TRR)	Minor Metabolites (<10%TRR)
Clover Foliage 0-DAT	Imazapyr	CL, 240,000 + CL 247,087; CL 252, 974; CL 9,140
Clover Foliage 4-DAT	Imazapyr	-
Clover Foliage 10-DAT	Imazapyr	CL, 240,000 + CL 247,087; CL 252, 974; CL 9,140
Clover Foliage 15-DAT	Imazapyr	CL, 240,000 + CL 247,087; CL 252, 974; CL 9,140
Clover Foliage 21-DAT	Imazapyr; CL, 240,000 + CL 247,087	CL 252, 974; CL 9,140

[Pyridine-6-^{14}C]-imazapyr was slowly metabolized in clover. The majority of the applied radioactivity remained as unchanged parent up to 21 days after treatment. The sites of metabolic transformation in clover are the carboxylic acid and imidazolinyl moieties of imazapyr. The metabolites CL 240,000 and/or a cyclization product, CL 247,087 were formed by esterification of the carboxylic acid moiety of imazapyr. The metabolite CL 252,974 (dicarbonyl-substituted nicotinic acid) was formed by opening of the imidazolinyl ring of imazapyr hydrolytically, and was further oxidized to pyridine CL 9,140 (dicarboxylic acid).

Proposed Metabolic Pathway of [Pyridine-6-^{14}C]-Imazapyr in Clover



CONFINED ACCUMULATION IN ROTATIONAL CROPS – Lettuce, radish, soybean and wheat		PMRA # 1843027
Radiolabel Position	[pyridine-6-^{14}C]-imazapyr	
Test site	The study was conducted under field conditions. Two plots (one control and one treated) were established at the test site. Corn seed was planted in sandy loam soil. Mature corn plants (primary crop) were harvested at maturity. The secondary crops were seeded 120 days after treatment of the primary crop (120-DAT) (winter wheat); 271-DAT (soybean, radish and lettuce); and 420-DAT (radish and lettuce). Samples of immature and mature commodities of each crop were harvested.	
Formulation used for trial	Imazapyr was formulated with water and non-ionic spreader, and applied as an aqueous ammonium salt solution.	
Application rate and timing	A single broadcast foliar application was made at 28 g a.e./ha to corn plants (primary crop) at the 6-leaf growth stage (22 days after planting of the corn seed).	
Metabolites Identified	**Major Metabolites (> 10% TRR)**	**Minor Metabolites (< 10% TRR)**
The total radioactive residues were less than the limit of detection (<0.002 ppm) in wheat forage, straw and grain 120-DAT; in immature and mature radish tops and roots, immature and mature lettuce and soybean forage, hay/hulls and seed 271-DAT; and in immature and mature radish tops and roots, and immature and mature lettuce 420-DAT.		

NATURE OF THE RESIDUE IN LAYING HEN	PMRA #1858914

Laying hens were dosed orally with [pyridine-6-^{14}C]-imazapyr at 1.98 ppm (n = 8) or 9.72 ppm (n = 8) based on the mean daily feed consumption for seven consecutive days. The control group (n = 8) was dosed with a capsule containing lactose. Samples of eggs (AM and PM) and excreta were collected daily. A blood sample was taken immediately prior to sacrifice. Animals were sacrificed approximately 22 hours after the final dose. Samples of liver, kidney, muscle, and skin with adhering fat were collected from each hen.

The total radioactive residues (TRRs) were less than the limit of detection (<0.01 ppm) in muscle, liver, kidney, skin with adhering fat, eggs and blood, and therefore were not further analyzed. Samples of excreta collected on Day 1 and Day 7 of dosing from both treatment groups were extracted and analyzed. The predominant residue was imazapyr, accounting for 92.5-96.1% of the TRRs.

The % of the administered dose were reported only for excreta.

Matrices	**% of Administered Dose**	
	1.98 ppm	**9.72 ppm**
Excreta (Day-7)	90.5	91.7

The results of the hen metabolism study indicate that the majority of the administered dose was excreted, with no concentration in the eggs and tissues.

NATURE OF THE RESIDUE IN LACTATING GOAT	PMRA # 1858912, 1858915

Pyridine Label

Lactating dairy goats were dosed orally with [pyridine-6-^{14}C]-imazapyr at 17.7 ppm (n = 1) or 42.5 ppm (n = 1) based on the mean daily feed consumption for seven consecutive days. The control animal was dosed with a capsule containing lactose. Milk was collected (AM and PM) daily and composited. Urine and feces were collected daily. Animals were sacrificed approximately 22 hours after the final dose. Samples of liver, kidney, muscle (leg and loin) and omental fat were collected from each goat. Samples of blood were collected on Days 0, 1, 3 and 7 days prior to the daily dose. Based on the distribution of radioactivity in goat matrices, only kidney and milk (Day-7 dosing) samples from the animal dosed at the high rate were subjected to extraction and subsequent chromatographic analysis.

Imidazole Label

A lactating dairy goat was dosed orally with [imidazole-5-^{14}C]-imazapyr at 46.87 ppm based on the mean daily feed consumption for seven consecutive days. The control animal was dosed with a capsule containing lactose. Milk was collected (AM and PM) daily and composited. Urine and feces were collected daily. Animals were sacrificed approximately 22 hours after the final dose. The only tissue collected was kidney given that the study conducted previously with pyridine labeled imazapyr showed that kidney and milk were the edible matrices that contained detectable residues.

The % of the administered dose were reported only for urine and feces.

Matrices	**% of Administered Dose**			
	[pyridine-6-^{14}C]-imazapyr		**[imidazole-5-^{14}C]-imazapyr**	
	17.7 ppm	**42.5 ppm**	**46.87 ppm**	
Urine	65.32	60.35	58.7	
Feces	16.11	18.97	34.4	
Urine and Feces (cumulative)	81.43	79.32	93.1	
	Major Metabolite (>10% TRR)	**Minor Metabolite (<10% TRR)**	**Major Metabolite (>10% TRR)**	**Minor Metabolite (<10% TRR)**
Radiolabel Position	**[pyridine-6-^{14}C]-imazapyr**		**[imidazole-5-^{14}C]-imazapyr**	
Kidney	imazapyr	-	imazapyr	-
Milk (Day-7)	imazapyr	-	imazapyr	-

The results of the lactating goat metabolism studies indicate that the majority of the administered dose was eliminated in the urine and to a lesser extent in the feces. Radioactive residues were detected above the detection limit only in kidney and milk from both studies. The predominant residue identified in kidney and milk with was imazapyr. No other metabolites were identified in milk and kidney.

STORAGE STABILITY- CORN COMMODITIES	PMRA # 1843021

Untreated control samples of corn grain, forage and fodder were spiked with imazapyr at 1.0 ppm. Duplicate treated samples of each matrix and one untreated control sample were stored frozen (-26 to -5^{o}C) and analyzed after 9, 12, 18 and 27 months of freezer storage. The results indicate that residues of imazapyr are stable in corn grain, forage and fodder when stored for up to 27 months of freezer storage.

STORAGE STABILITY- LIVESTOCK COMMODITIES

Given that finite residues of imazapyr are not anticipated from the uses on Clearfield canola, Clearfield canola quality *Brassica juncea* and Clearfield lentils, data demonstrating the stability of imazapyr residues in livestock matrices are not required at this time.

CROP FIELD TRIAL ON CROP SUBGROUP 20A (RAPESEED SUBGROUP)	PMRA # 1843006

During the 2008 growing season a sufficient number of trials were conducted in Canada in representative growing regions to evaluate the magnitude of imazapyr and imazamox in/on Clearfield canola (representative crop of Crop Subgroup 20A).

The end-use product BAS 723 00 H, a liquid formulation of the co-actives imazamox and imazapyr, was applied using ground equipment once to Clearfield canola at 20-21 g a.e./ha (imazamox) and 9-10 g a.e./ha (imazapyr). The growth stage of canola at the time of application ranged from the 4-leaf to 50% bloom. An adjuvant was added to the spray mixture for all applications (Merge, 0.5% v/v). At each site, 1 control and duplicate canola seed RAC (raw agricultural commodity) samples were harvested by hand or using mechanical equipment. Mature dry canola seed samples were harvested 68-72 days after treatment (DAT). At one site, additional samples of seed were collected at 49, 60, 80 and 90 DAT to evaluate residue decline.

Residues of imazapyr in/on seed were quantitated by LC-MS/MS (liquid chromatography with tandem mass spectrometry) using BASF Method M 3519, with minor modifications. The limit of quantitation (LOQ) was reported as 0.05 ppm for each analyte.

Residue decline could not be determined as residues of imazapyr were non-quantifiable at each of the sampling intervals.

Commodity	Total Applic. Rate (g a.e./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
	9-10	**Imazapyr**							
		68-72	24	<0.05	<0.05	<0.05	<0.05	<0.05	0

CROP FIELD TRIAL ON LENTILS	PMRA # 1843005

During the 2008 growing season a sufficient number of trials were conducted in Canada in representative growing regions to evaluate the magnitude of imazapyr and imazamox in/on Clearfield lentils.

The end-use product BAS 723 00 H, a liquid formulation of the co-actives imazamox and imazapyr, was applied using ground equipment once to lentils at 19-20 g a.e./ha (imazamox) and 9 g a.e./ha (imazapyr). The growth stage of lentils at the time of application ranged from stem elongation (6-8 nodes) to early flowering. An adjuvant (Merge; 0.5% v/v) was included in all spray applications. Mature dry lentil seed samples were harvested 58-60 DAT. At one site, additional samples of seed were collected at 40, 50, 70 and 81 DAT to evaluate residue decline.

Residues of imazapyr in/on lentil seed were quantitated by LC-MS/MS using BASF Method M 3519, with minor modifications. The LOQ was reported as 0.05 ppm for each analyte.

The residue decline data indicated that residues of imazapyr remained relatively constant.

Commodity	Total Applic. Rate (g a.e./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Lentil Seed	9	**Imazapyr**							
		58-60	10	0.06	0.10	0.08	0.06	0.066	0.013

FIELD ACCUMULATION IN ROTATIONAL CROPS	
Based on the results of the confined rotational study, finite residues of imazapyr are not anticipated in/on any commodities at the shortest plank-back interval of 120 days.	
PROCESSED FOOD AND FEED-CANOLA	**PMRA # 1843006**
Test Site	Waldheim, Saskatchewan
Treatment	Single broadcast foliar application using ground equipment.
Rate	45 g a.e./ha for imazapyr; 100 g a.e./ha for imazamox
End-use product	BAS 723 00 H, a liquid formulation containing 31.3 g/L imazamox and 14.2 g/L imazapyr
PHI	70 days
Processed Commodity	**Processing Factor**
	Imazapyr
Meal	1.4-fold
Refined Oil	<0.7-fold
LIVESTOCK FEEDING	
The only feed commodity associated with the proposed uses on Clearfield canola, Clearfield canola quality *Brassica juncea* and Clearfield lentils is canola meal, which can potentially be fed to cattle, hogs and poultry (DIR98-02). The anticipated residues in canola meal were calculated as follows: HAFT in seed (0.05 ppm = LOQ) x 1.4-fold (meal processing factor)) = 0.07 ppm. The dietary burden was estimated to be 0.01 ppm for swine, poultry and dairy cattle, and 0.00 ppm for beef cattle. Based on the results of the goat and poultry metabolism studies, which were conducted at highly exaggerated rates and the estimated dietary burdens, finite residues of imazapyr are not anticipated in the meat, milk and eggs.	

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

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (cereal, pulses and oilseeds)** **Rotational crops**	 Imazapyr Imazapyr
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops (cereals, pulses and oilseeds)** **Rotational crops**	 Imazapyr Imazapyr
METABOLIC PROFILE IN DIVERSE CROPS	The profile in diverse crops cannot be determined because only cereals and pulses/oilseeds were investigated.
ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT	Imazapyr
RESIDUE DEFINITION FOR RISK ASSESSMENT	Imazapyr
METABOLIC PROFILE IN ANIMALS **(goat, hen, rat)**	Yes

FAT SOLUBLE RESIDUE		No	
DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic non-cancer dietary risk **ADI = 2.53 mg/kg bw/day** **Estimated chronic drinking water concentration = 2.0 μg a.i./L (Level 2, groundwater)**	**All infants < 1 year**	0.00	0.00
	Children 1–2 years	0.00	0.00
	Children 3 to 5 years	0.00	0.00
	Children 6–12 years	0.00	0.00
	Youth 13–19 years	0.00	0.00
	Adults 20–49 years	0.00	0.00
	Adults 50+ years	0.00	0.00
	Females 13–49 years	0.00	0.00
	Total population	0.00	0.00

Table 7 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (cereal, pulses and oilseeds)** **Rotational crops**	 Imazapyr Imazapyr
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops (cereals, pulses and oilseeds)** **Rotational crops**	 Imazapyr Imazapyr
METABOLIC PROFILE IN DIVERSE CROPS	The profile in diverse crops cannot be determined because only cereals and pulses/oilseeds were investigated.
ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT	Imazapyr
RESIDUE DEFINITION FOR RISK ASSESSMENT	Imazapyr
METABOLIC PROFILE IN ANIMALS (goat, hen, rat)	Yes
FAT SOLUBLE RESIDUE	No

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic non-cancer dietary risk **ADI = 2.53 mg/kg bw/day** **Estimated chronic drinking water concentration = 2.0 μg a.i./L (Level 2, groundwater)**	**All infants < 1 year**	0.00	0.00
	Children 1–2 years	0.00	0.00
	Children 3 to 5 years	0.00	0.00
	Children 6–12 years	0.00	0.00
	Youth 13–19 years	0.00	0.00
	Adults 20–49 years	0.00	0.00
	Adults 50+ years	0.00	0.00
	Females 13–49 years	0.00	0.00
	Total population	0.00	0.00

Table 8 Toxicity of Imazapyr (TGAI) and Imazapyr-Imazamox formulation (EP) to Non-Target Species. These endpoints are taken from newly submitted and reviewed studies for the proposed use expansion of Imazapyr.

Organism	Exposure	Value	Reference
Invertebrates			
Earthworm	EP, Acute	14-d LD_{50} > 100 mg formulation/kg dry soil This is equivalent to 14.23 mg Imazapyr/kg dry soil and 30.78 mg Imazamox/kg dry soil	PMRA# 1858998
Bees	EP, Acute Contact	LD_{50} > 100 µg formulation/bee This is equivalent to 112 kg formulation/ha, 1.57 kg Imazapyr/ha and 3.44 mg Imazamox/ha	PMRA# 1859001
	EP, Acute Oral	LD_{50} >117 µg formulation/bee This is equivalent to 131 kg formulation/ha, 1.83 kg Imazapyr/ha and 4.03 mg Imazamox/ha	
Birds			
Bobwhite quail	EP, Acute	LD_{50} > 2025 mg formulation/kg bw NOEL = 2025 mg formulation/kg bw This is equivalent to 28.8 mg Imazapyr/kg bw.	PMRA# 1859058
	TGAI, Reproduction	NOEC = 1800 mg a.i./kg diet This is equivalent to a daily dose of 149.4 mg Imazapyr/kg bw/day	PMRA# 1859072
Mallard duck	TGAI, Reproduction	NOEC = 1800 mg a.i./kg diet This is equivalent to a daily dose of 257.0 mg Imazapyr/kg bw/day	PMRA# 1859070

Organism	Exposure	Value	Reference
Freshwater species			
Freshwater invertebrate *Daphnia magna*	EP, Acute	EC_{50} > 100 mg formulation/L NOEC = 100 mg formulation/L This is equivalent to 1.39 mg Imazapyr/L and 3.07 mg Imazamox/L	PMRA# 1859018
Cold water fish Rainbow trout	EP, Acute	LC_{50} > 100 mg formulation/L NOEC = 100 mg formulation/L This is equivalent to 1.39 mg Imazapyr/L and 3.07 mg Imazamox/L	PMRA# 1859039
Freshwater alga (*Selenastrum capricornutum*)	EP, Acute	EC_{50} > 100 mg formulation/L NOEC = 100 mg formulation/L This is equivalent to 1.39 mg Imazapyr/L and 3.07 mg Imazamox/L	PMRA# 1859073

Table 9 Screening Level Risk Assessment on non-target terrestrial organisms other than birds and mammals.

Organism	Exposure	Endpoint value	Imazapyr EEC	RQ
Invertebrates				
Earthworm	EP, Acute	NOEC > 133 mg a.i./kg soil	0.004 mg a.i./kg soil	0.00003
	EP, Acute	LD_{50} > 14.23 mg a.i./kg soil	0.004 mg a.i./kg soil	0.00028
Bee	TG, Contact	LD_{50} > 112 kg a.i./ha	9.0 g a.i./ha	0.00008
	EP, Contact	LD_{50} >112 kg a.i./ha	9.0 g a.i./ha	0.00008
	EP, Oral	LD_{50} > 1.83 kg a.i./ha	9.0 g a.i./ha	0.00492
	EP, Contact	LD_{50} > 1.57 kg a.i./ha	9.0 g a.i./ha	0.00573
Vascular plants				
Vascular plant	Seedling emergence	EC_{25} = 2.70 g a.i./ha (sugarbeet)	Screening level: 9.0 g a.i./ha	**3.333**
			Refinement: 0.54 g a.i./ha (6% spray drift)	0.200
	Vegetative vigour	EC_{25} = 1.01 g a.i./ha (cucumber)	Screening level: 9.0 g a.i./ha	**8.911**
			Refinement: 0.54 g a.i./ha (6% spray drift)	0.535

Table 10 Screening Level Risk Assessment on non-target terrestrial birds and mammals.

Organism and Exposure	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	On-field Imazapyr EDE (mg a.i./kg bw)	On-field RQ
Small Bird (0.02 kg)				
Acute	215.00	Insectivore (small insects)	0.45	0.0021
Reproduction	149.40	Insectivore (small insects)	0.45	0.0030
Medium Sized Bird (0.1 kg)				
Acute	215.00	Insectivore (small insects)	0.35	0.0016
Reproduction	149.40	Insectivore (small insects)	0.35	0.0024
Large Sized Bird (1 kg)				
Acute	215.00	Herbivore (short grass)	0.37	0.0017
Reproduction	149.40	Herbivore (short grass)	0.37	0.0025
Small Mammal (0.015 kg)				
Acute	500.00	Insectivore (small insects)	0.26	0.00052
Reproduction	700.00	Insectivore (small insects)	0.26	0.00037
Medium Sized Mammal (0.035 kg)				
Acute	500.00	Herbivore (short grass)	0.82	0.00163
Reproduction	700.00	Herbivore (short grass)	0.82	0.00117
Large Sized Mammal (1 kg)				
Acute	500.00	Herbivore (short grass)	0.44	0.00087
Reproduction	700.00	Herbivore (short grass)	0.44	0.00062

Table 11 Screening Level Risk Assessment on non-target aquatic organisms.

Organism	Exposure	Endpoint value	Imazapyr EEC (mg a.i./L)	RQ
Freshwater species				
Daphnia magna	TGAI, Acute	½ EC_{50} > 50 mg a.i./L	0.0011	0.00002
	EP, Acute	½ EC_{50} = 39.5 mg a.i./L	0.0011	0.00003
	EP, Acute	½ EC_{50} > 0.695 mg a.i./L	0.0011	0.00158
Rainbow trout	TGAI, Acute	1/10 LC_{50} > 10 mg a.i./L	0.0011	0.00011
	EP, Acute	1/10 LC_{50} = 2.49 mg a.i./L	0.0011	0.00044
	EP, Acute	1/10 LC_{50} > 0.139 mg a.i./L	0.0011	0.00791
Bluegill sunfish	TGAI, Acute	1/10 LC_{50} > 10 mg a.i./L	0.0011	0.00011
	EP, Acute	1/10 LC_{50} = 4.07 mg a.i./L	0.0011	0.00027
Channel catfish	TGAI, Acute	1/10 LC_{50} > 10 mg a.i./L	0.0011	0.00011
Amphibian	Acute	1/10 LC_{50} > 0.139 mg a.i./L	0.006	0.04317
Freshwater alga	TGAI, Acute	*A. flos-aquae* ½ EC_{50} = 6.1 mg a.i./L	0.0011	0.00018
	TGAI, Acute	*S. capricornutum* ½ EC_{50} = 35.5 mg a.i./L	0.0011	0.00003
	EP, Acute	*S. capricornutum* ½ EC_{50} = 7.05 mg a.i./L	0.0011	0.00016
	EP, Acute	*S. capricornutum* ½ EC_{50} > 0.695 mg a.i./L	0.0011	0.00158
Vascular plant *Lemna gibba*	TGAI, Acute	½ EC_{50} = 0.012 mg a.i./L	0.0011	0.09167
	EP, Acute	½ EC_{50} = 0.0108 mg a.i./L	0.0011	0.10185
Marine species				
Crustacean Pink shrimp	TGAI, Acute	½ LC_{50} > 94.5 mg a.i./L	0.0011	0.00001
Mollusk Eastern oyster	TGAI, Acute	½ LC_{50} > 66 mg a.i./L	0.0011	0.00002
Salmonid Atlantic silverside	Acute	1/10 LC_{50} > 18.4 mg a.i./L	0.0011	0.00006
Marine alga	TGAI, Acute	*S. costatum* ½ EC_{50} = 42.75 mg a.i./L	0.0011	0.00003

Table 12 Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

Applicant proposed label claims	Accepted label claims	Unsupported label claims
Applic. rate: 29 g a.i./ha (20 g/ha imazamox + 9 g/ha imazapyr)	- accepted as proposed	
Adjuvant: Merge Adjuvant at 0.5% v/v (e.g., 5 L Merge Adjuvant per 1000 L spray solution)	- accepted as proposed	
Pest Claims: **i) Grassy weeds (1-6 true leaf stage with up to 2 tillers):** Barnyard grass Green foxtail Spring germinating Japanese brome grass[1] Wild oats Yellow foxtail Persian darnel Vol. canary seed Vol. durum wheat Vol. barley Vol. tame oats Vol. spring wheat (non-imazamox tolerant wheat) **ii) Broadleaf weeds (cotyledon to 4 leaf stage):** Cleavers Cow cockle Green smartweed Hemp-nettle Lamb's quarters[2] Redroot pigweed Shepherd's purse Stinkweed Wild buckwheat[2] Wild mustard Vol. canola (non-clearfield canola varieties only) Vol. tame mustard [1] Japanese brome grass (1-4 leaf stage) [2] Lamb's quarters & Wild buckwheat (cotyledon to 6-leaf stage)	- accepted as proposed	

Applicant proposed label claims	Accepted label claims	Unsupported label claims
Crop Claims: **i) Ares + Merge:** Clearfield canola (2-7 leaf stage) Clearfield canola quality *Brassica juncea* (2-7 leaf stage) Clearfield lentil (1-9 node stage) **ii) Ares + Merge + Lontrel 360 or Lontrel Dry:** Clearfield canola (2-6 leaf stage) **iii) Ares + Equinox EC + Merge:** Clearfield canola (2-7 leaf stage) Clearfield canola quality *Brassica juncea* (2-7 leaf stage) Clearfield lentil (1-9 node stage)	**i) Ares + Merge:** - accepted as proposed **ii) Ares + Merge + Lontrel 360 or Lontrel Dry:** - accepted as proposed **iii) Ares + Equinox EC + Merge:** - accepted as proposed	
Method of Applic.: Apply using ground equipment only. DO NOT APPLY BY AIR.	- accepted as proposed	
Rotational Crop Claims: **1 year after application:** Canary seed chickpeas Durum wheat Field peas Field corn Clearfield canola Clearfield juncea Lentils including Clearfield lentils Spring wheat including Clearfield spring wheat Spring barley Tame oats **2 years after application:** Canola Flax Sunflower	- accepted as proposed with one exception. The reference to 'Clearfield juncea' must be replaced with 'Clearfield canola quality *Brassica juncea*'	
No. Applic. Per Year: DO NOT apply more than once per year.	- accepted as proposed	
Misc.: - national registration	- Prairie Provinces and Peace River Region of British Columbia only	

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

Table 1 Differences Between MRLs in Canada and in Other Jurisdictions

As per Table 1, the proposed MRLs for dry lentils and the rapeseed subgroup (Crop Subgroup 20A) in Canada are different from the ones established in the US (tolerances are listed in 40 CFR Part 180). With respect to the proposed MRLs for livestock commodities in Canada, there are no tolerances established in the US for poultry and hog commodities. There is a separate tolerance established in the US for imazapyr in/on kidney. There are no CODEX MRLs established for imazapyr in/on any commodity as this time (Codex MRLs searchable by pesticide or commodity).

Table 1 Differences Between Canadian MRLs and in Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Dry lentils	0.2	No tolerance established	No MRL established
Kidney of cattle, goat, horse and sheep	-	0.20	No MRL established
Meat byproducts of cattle, goats, hogs, horses, poultry and sheep	0.05	-	No MRL established
Eggs	0.05	No tolerance established	No MRL established
Rapeseed subgroup (Crop Subgroup 20A)	0.05	No tolerance established	No MRL established

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

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

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

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A. List of Studies/Information Submitted by Registrant

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