Proposed Re-evaluation Decision PRVD2015-04

# Imazamox

*(publié aussi en français)*

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# Overview

## What is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide imazamox, the Health Canada Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing imazamox for sale and use in Canada.

An evaluation of available scientific information found that products containing imazamox do not present unacceptable risks to human health or the environment when used according to the revised label directions. As a condition of the continued registration of imazamox uses, new risk-reduction measures are proposed to be included on the labels of all products.

This proposal affects all end-use products containing imazamox registered in Canada. Once the final re-evaluation decision is made, the registrant will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for imazamox and presents the reasons for the proposed re-evaluation decision.

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

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

## What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2012-02, Re-evaluation Program Cyclical Re-evaluation, presents the details of the cyclical re-evaluation approach, which is in line with the requirements of the *Pest Control Products Act*.

## What is Imazamox?

Imazamox is a selective post-emergence herbicide. It is registered for the control of broadleaf and grassy weeds in crops with an imidazolinone tolerance (naturally occurring or Clearfield trait). Imazamox is used in the Prairie Provinces, and Peace River region of British Columbia, on Clearfield crops (wheat, canola, canola quality *Brassica juncea*, lentils and sunflowers) and field

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

peas, dry edible beans (tank mix only), fenugreek for seed and forage uses, seedling and established alfalfa grown for seed, and bird's foot trefoil for seed production. It is also used on soybeans in Western Canada (Prairie Provinces and Peace River region of British Columbia) and Eastern Canada. Imazamox products are formulated as a solution, emulsifiable concentrate or water dispersible granules. Commercial-class products containing imazamox can be applied once per year using a ground sprayer. There are no domestic-class products containing this active ingredient.

## Health Considerations

### Can Approved Uses of Imazamox Affect Human Health?

**Imazamox is unlikely to affect your health when used according to the revised label directions.**

People could be exposed to imazamox by working as a mixer/loader/applicator, by entering treated sites, or by consuming food and water. PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Occupational exposures of workers mixing, loading and applying the herbicide using a ground sprayer, as well as workers re-entering treated sites, are not of concern under current conditions of use. There are no residential uses of imazamox nor is it expected that commercial application would occur in residential areas. Exposure to bystanders from spray drift is addressed through best management practice label statements and is not expected to be of concern. Dietary exposure to imazamox through consumption of food commodities and drinking water is also not of concern. Additional label statements are proposed to be added to the product labels for re-entry to treated sites and for the protection of bystanders.

### Maximum Residue Limits

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

MRLs for imazamox have been established for the registered commodities.

## Environmental Considerations

### What Happens When Imazamox is Introduced Into the Environment?

**Imazamox is toxic to non-target terrestrial plants; therefore, additional risk-reduction measures are required.**

Once applied to fields, imazamox is slightly to moderately persistent in the terrestrial environment. If it enters aquatic systems, it is likely to be persistent. It is not expected to partition into air or result in long-range transport. Some characteristics of imazamox from laboratory studies indicate that it may be mobile in soils and could enter groundwater; however, limited downward movement was observed in field studies.

Imazamox is not toxic to earthworms, bees, birds, terrestrial mammals, marine and freshwater invertebrates or fish, and the use of imazamox does not pose a risk to these biota. Imazamox is toxic to non-target terrestrial plants and the use of imazamox at registered application rates poses a risk to terrestrial plants. To reduce exposure to non-target plants, additional risk-reduction measures (label statements and buffer zones) are required.

## Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of imazamox, PMRA is proposing further risk-reduction measures related to human health and the environment for product labels.

### Human Health

- Restricted entry interval of 12 hours.
- Precautionary label statement to minimize bystander exposure from spray drift.

### Environment

- Buffer zone and label statements to protect non-target terrestrial plants.
- Environmental hazard label statements.

A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

## What Additional Scientific Information is Required?

No additional data are required.

## Next Steps

Before making a final re-evaluation decision on imazamox, PMRA will consider all comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on imazamox. PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA response to these comments.

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

# Science Evaluation

## 1.0 Introduction

Imazamox is a selective, systemic, post-emergence herbicide registered for the control of broadleaf and grass weeds in crops with an imidazolinone tolerance.

Following the re-evaluation announcement for imazamox, the registrant of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses included on the label of the commercial class end-use products in Canada.

Currently registered products containing imazamox are listed in Appendix I.

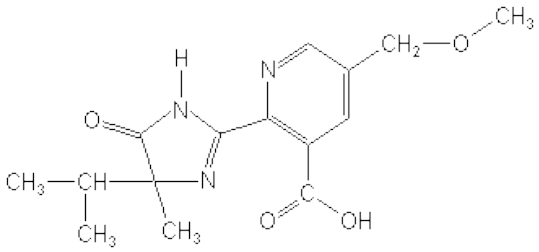
## 2.0 Use Description of Imazamox

Imazamox is a post-emergence herbicide registered in Canada for use on soybean, Clearfield wheat, Clearfield canola, Clearfield canola quality *Brassica juncea*, Clearfield lentils, Clearfield sunflowers, field peas, dry edible beans, fenugreek for seed and forage uses, seedling and established alfalfa grown for seed, and bird's foot trefoil for seed production. Imazamox can be applied once per year using a groundboom.

## 3.0 The Technical Grade Active Ingredient and Its Properties

### 3.1 Identity of the Technical Grade Active Ingredient

| | |
|---|---|
| **Common Name** | Imazamox |
| **Function** | Herbicide |
| **Chemical Family** | Imidazolinone |
| **Chemical Name** | |
| **1 International Union of Pure and Applied Chemistry (IUPAC)** | 2-[(*RS*)-4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl]-5-methoxymethylnicotinic acid |
| **2 Chemical Abstracts Service (CAS)** | 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-(methoxymethyl)-3-pyridinecarboxylic acid |
| **CAS Registry Number** | 114311-32-9 |
| **Molecular Formula** | $C_{15}H_{19}N_3O_4$ |
| **Molecular Weight** | 305.3 |

| | |
|---|---|
| **Structural Formula** |  |
| **Purity of the Technical Grade Active Ingredient** | 97% nominal |
| **Registration Number** | 25109 |

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

### 3.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

| Property | Result | Interpretation |
|---|---|---|
| Vapour pressure | < $1.3 \times 10^{-2}$ mPa | Low volatility. |
| UV Ultraviolet/Visible spectrum | No absorption at λ >350 nm | Phototransformation is unlikely. |
| Solubility in water | **pH** **(g/L)**<br>5 116<br>7 > 626<br>9 > 628<br>Deionized water 4160 ppm (20ºC) | Very soluble in water. |
| *n*-Octanol–water partition coefficient ($K_{ow}$) | **pH** **log $K_{ow}$**<br>5 -1.03 (uncorrected for dissociation)<br>7 -2.4 (uncorrected for dissociation)<br>5, 6 0.73 (corrected for dissociation) | Bioaccumulation is unlikely. |
| Dissociation constant (p$K_a$) | p$Ka_{1,2,3}$ = 2.3, 3.3, 10.8 | Mobility in soil increases as soil pH increases. |

## 4.0 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans. It is also assumed that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to imazamox may occur through consuming food and drinking water, working as a mixer/loader/applicator, or by entering treated sites.

When assessing health risks, PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers).

## 4.1 Toxicological Summary

The database for imazamox is considered complete and no data deficiencies have been identified by PMRA.

Imazamox is rapidly absorbed and excreted. It is primarily excreted in the urine as the parent compound. Imazamox has low acute oral, dermal and inhalation toxicity. It is mildly irritating to the eyes and slightly irritating to the skin. Imazamox is not a skin sensitizer.

No treatment-related effects were observed following short-term dietary exposure of rats or dogs, or dermal exposure of rats, to imazamox up to the highest doses tested.

In long-term dietary toxicity/carcinogenicity, there were no treatment-related effects. There was no evidence of oncogenic/carcinogenic potential of imazamox following exposure to imazamox in mice and in rats up to the highest dose tested. Imazamox is not considered to be mutagenic or genotoxic. In the absence of evidence of oncogenicity or genotoxicity, a cancer-risk assessment was not required for imazamox.

There was no evidence of reproductive or developmental toxicity in rats observed up to the limit dose, or in a developmental toxicity study in rabbits at the highest doses tested.

Standard 10-fold uncertainty factors for intraspecies and interspecies extrapolation have been applied for calculation of the target margin of exposure (MOE). As the no observed adverse effect levels (NOAELs) used are the highest dose tested, there is no common endpoint to combine in the exposure assessment. No additional toxicology data is required for re-evaluation.

## 4.2 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This takes 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, the database contains the full complement of required studies including developmental toxicity studies in rats and rabbits and a multi-generation 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. No adverse effects were observed in the rat reproductive or developmental toxicity studies. No adverse effects were observed in the rabbit developmental toxicity study. On the basis of this information, the *Pest Control Products Act* factor was reduced to one-fold.

Appendix II provides an overview of imazamox toxicology endpoints used in human-health risk assessments by PMRA.

### 4.3 Dermal Absorption

Since a 28-day dermal rat study was used to determine the toxicological endpoints, a dermal absorption factor for imazamox is not required.

### 4.4 Occupational Exposure

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a MOE. This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Workers can be exposed to imazamox through mixing, loading or applying the product using a groundboom sprayer or when entering a treated site to conduct activities such as scouting and/or handling treated crops.

#### 4.4.1 Mixer/Loader/Applicator Exposure and Risk

Mixer/loader/applicator exposure is expected to be mainly via dermal and inhalation routes. Based on the imazamox use pattern, the following scenarios were assessed:

- Short- and intermediate-term exposure from open mixing/loading of water dispersible granule (WDG) formulation and application using an open cab groundboom sprayer.
- Short- and intermediate-term exposure from open mixing/loading of liquid formulation and application using an open cab groundboom sprayer.

Exposure for workers mixing/loading a WDG or a liquid formulation and applying the pesticide using an open cab groundboom sprayer was estimated using unit exposure values from the Pesticide Handlers Exposure Database (PHED), version 1.1. It is assumed that workers were wearing personal protective equipment consisting of a single layer of clothing plus gloves. The assessments were based on maximum application rates and assuming an area treated per day up to 360 ha.

The combined short- to intermediate-term dermal and inhalation MOEs for WDGs and liquid formulations were above the target MOE. On this basis, the risk for workers mixing, loading and applying the herbicide using a groundboom sprayer is not of concern.

Requirements for personal protective equipment included on current product labels are adequate and no additional mitigation measures are proposed.

### 4.4.2 Post-application Exposure and Risk

For workers entering treated fields to conduct post-application activities, dermal exposure is considered to be the primary route of exposure. Imazamox is relatively non-volatile (vapour pressure of $9.7 \times 10^{-8}$ mm Hg at 25°C). It meets the North American Free Trade Agreement (NAFTA) criterion for an inhalation waiver based on low volatility due to a vapour pressure of less than $7.5 \times 10^{-4}$ mm Hg (NAFTA, 1999). Therefore, inhalation exposure is considered minimal and is not expected to be of concern for post-application activities.

Dermal exposure estimates for post-application workers were calculated assuming dislodgeable foliar residue values based on a single application at the maximum application rate and activity-specific transfer coefficients. The estimated dermal MOEs were above the target MOE on the day of application. This indicated that the post-application risk for workers entering treated fields is not of concern, provided a restricted entry interval of 12 hours is established.

Therefore, a label amendment is proposed to specify a restricted entry interval of 12 hours for all product labels. The proposed label statements are listed in Appendix III.

## 4.5 Non-occupational Exposure

### 4.5.1 Residential Exposure and Risk

There are no residential uses of imazamox nor is it expected that the commercial products would be applied in residential areas. A standardized statement is proposed to specify that application is limited to agricultural crops and should be applied when the spray is unlikely to drift into areas of human habitation or activity such as houses, cottages, schools and recreational areas. The proposed label statements are listed in Appendix III.

### 4.5.2 Dietary Exposure and Risk

In a dietary exposure assessment, PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet (food and drinking water). These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults.

The residue definition of imazamox in plants and animals is the parent compound only, imazamox: 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1*H*-imidazol-2-yl]-5-(methoxymethyl)-3-pyridinecarboxylicacid.

An acute reference dose for imazamox was not determined since a toxicological endpoint of concern attributable to a single dose was not identified. Therefore, an acute dietary exposure assessment was not required.

The chronic dietary exposure was calculated by using the average consumption of different foods and the estimated residue values of imazamox on those foods. The expected intake of residues was then compared to the acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the expected intake of residues is less than the acceptable daily intake, then chronic dietary exposure is not of concern.

Residue estimates used in the dietary risk assessment were conservatively based on Canadian MRL level residues.

The acceptable daily intake for imazamox was determined to be 8.7 mg/kg bw/day (see Appendix II). The basic chronic dietary exposure to imazamox from food alone, and from food plus water, for the general population and for all subpopulations represented less than 1% and 10% of the acceptable daily intake, respectively. On this basis, it is concluded that dietary exposure to imazamox residues is not of concern.

### 4.6 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

For imazamox, aggregate exposure is limited to food and drinking water only. Aggregate dietary exposure from food and drinking water is considered acceptable and below the level of concern, for all population subgroups.

### 4.7 Cumulative Exposure and Risk

Imazamox is a member of the imidazolinone class of pesticides, which inhibit the acetolactate synthase enzyme in plants. Imazamox did not elicit any treatment-related effects of toxicological concern in any of the animal studies conducted. No common mechanism of toxicity applicable to humans or animals has been found with other pest control products. Therefore, no cumulative risk assessment was conducted during the re-evaluation.

# 5.0 Environment

## 5.1 Environmental Fate

Based on its vapour pressure, imazamox is not expected to volatilize into the air after application or be susceptible to long-range transport. Imazamox is very soluble in water and is stable to hydrolysis. Bioaccumulation is not expected based on the log octanol-water partition coefficient. The mobility of imazamox in soil increases as soil pH increases. Imazamox is not expected to breakdown via photolysis.

Laboratory studies indicate that imazamox is persistent in aerobic soil (dissipation time, $DT_{50}$ of 76 days and $DT_{90}$ of 528 days at 25ºC [biphasic degradation], and half-life of 660 days at 4ºC), aerobic water/sediment systems (estimated half-life of 975 days at 25ºC and 2336 days at 4ºC), and anaerobic water/sediment systems (half-life of 761 days at 25ºC and no transformation at 4ºC). Imazamox also has high to very high mobility in soil (adsorption partition coefficients [$K_{oc}$] range from 4 to 130). Therefore, there is potential for carryover of imazamox residues in use areas and it could potentially move into groundwater.

Results of field dissipation studies indicate slight to moderate persistence under field use conditions ($DT_{50}$ ranges from 20 to 55 days). Between 20% and 30% of imazamox (and its breakdown products) may not decompose prior to the next field application. In general, downward movement of imazamox was observed in the field studies when preceded by rainfall, indicating that with suitable environmental conditions soon after application, there is a potential for leaching of imazamox and its transformation products.

Canadian water monitoring data show that imazamox was detected in < 0.1% of surface water samples from two provinces. The maximum concentration detected was 9.09 µg/L, which is lower than the expected environmental concentration of 16.7 µg/L used in the environmental risk assessment. Detection in surface water in the United States was similar to surface water in Canada, with a frequency of detection of 0.3% with the highest concentration being 0.064 µg/L. Detection in finished water in the United States was 0.2% with the maximum detection of 0.017 µg/L. Imazamox was not detected in any of the groundwater samples from Canada or the United States.

## 5.2 Environmental Exposure and Risk Assessment

Based on the registered application rate, the expected environmental concentrations in soil and water are 11.1 µg/kg and 0.016 mg/L, respectively.

### 5.2.1 Terrestrial Organisms

Imazamox is not acutely toxic to the mallard duck or bobwhite quail via oral dose or in dietary toxicity studies. Reproduction in the mallard duck and bobwhite quail is also not affected when birds were exposed to imazamox in the diet. Imazamox is not acutely or chronically toxic to terrestrial mammals. Imazamox is not considered to be toxic to terrestrial invertebrates (including earthworms and bees).

Imazamox, when used at registered application rates, is not expected to adversely affect earthworms, bees and terrestrial invertebrates. Acute or reproductive risks for birds and mammals through on-field exposure are also not of concern.

Imazamox is acutely toxic to terrestrial plants based on plant stand, vigour, malformations, plant size and chlorosis, and risks were identified for non-target terrestrial plants. Therefore, buffer zones are required to protect non-target terrestrial plants. Further, revised environmental label statements are proposed for end-use products based on the current PMRA practices. The proposed label statements are listed in Appendix III.

### 5.2.2 Aquatic Organisms

Imazamox is not toxic to freshwater fish, algae, and freshwater or marine invertebrates on an acute or chronic basis. The risk assessment conducted at registered application rates of imazamox showed that there is no risk expected for these organisms. Based on this, no additional mitigation is required for protection of aquatic biota.

## 6.0 Value

Imazamox is a Group 2 herbicide. Although weed biotypes resistant to Group 2 herbicides have been well documented in Canada, imazamox has value in mitigating resistance development in weeds to other herbicide groups. Resistance management recommendations can be found on the Canadian imazamox end-use product labels.

## 7.0 Pest Control Product Policy Considerations

### 7.1 Toxic Substances Management Policy Considerations

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

During the re-evaluation process, imazamox was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and evaluated against the Track 1 criteria. PMRA has reached the following conclusion:

- Imazamox is found to persist in water/sediment (half-life > 761 days) and soil (half-life of 660 days). The half-life in soil and water is above the TSMP Track 1 criteria (half-life in water or soil ≥ 182 days or in sediment > 365 days), therefore it is concluded that imazamox does meet the criteria for persistence.

- The log $K_{ow}$ of 0.73 for imazamox is below the TSMP Track 1 criterion (log $K_{ow} \geq 5$). On this basis, it is concluded that imazamox does not meet the criteria for bioaccumulation.
- Imazamox does not meet all Track 1 criteria and therefore is not considered a Track 1 substance.

### 7.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of imazamox, contaminants in the technical grade active ingredient were compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[3] The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03 and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). PMRA has reached the following conclusion:

- Technical grade imazamox does not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

## 8.0 Incident Reports

Starting 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to PMRA within a set time frame.

As of 7 November 2014, PMRA had received two domestic animal incidents associated with imazamox. Both were classified as death, occurred in the United States, and were considered to be unlikely to be related to the reported exposure to imazamox. One scientific study incident was received, which tested the acute toxicity of an imazamox formulation in rainbow trout. In addition to the above mentioned incidents, 19 packaging failure incidents were reported.

The Ecological Incident Information System (EIIS) of the United States Environmental Protection Agency was queried for environmental imazamox incidents that were available in the database as of November 2013. There were five incidents reports available in the EIIS database. All incidents were considered to be at least possibly associated with the reported exposure. Plant damage was reported in all incidents and the product in all incidents was listed as Raptor. Four incidents involved field corn in which the route of exposure was listed as carryover. In three of these incidents, soybeans had been treated (two broadcast, one bait). There was one incident involving beans (unspecified) that had been treated directly (application method unspecified).

All relevant information received through the PMRA incident reporting program were considered in the re-evaluation of imazamox.

[3] *Canada Gazette*, Part II, Volume 139, Number 24, 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, 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.*

## 9.0 Organisation for Economic Co-operation and Development Status of Imazamox

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which provides a forum in which governments can work together to share experience and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries.

Imazamox is currently acceptable for use in other OECD countries, including the United States, Australia and European Union Member States. As of 7 November 2014, no decision by an OECD member country to prohibit all uses of imazamox for health or environmental reasons has been identified.

## 10.0 Proposed Re-evaluation Decision

PMRA has determined that products containing imazamox for sale and use in Canada are acceptable for continued registration with the implementation of the proposed label amendments (Appendix III).

## 11.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, and DACO tables (datacode tables) can be found on the Pesticides and Pest Management portion of the Health Canada website. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through the Environment Canada website.

# List of Abbreviations

| | |
|---|---|
| a.e. | acid equivalent |
| ASAE | American Society of Agricultural Engineers |
| bw | body weight |
| CAS | Chemical Abstracts Service |
| $DT_{50}$ | dissipation time 50% |
| EIIS | Ecological Incident Information System |
| g | gram(s) |
| h | hectare(s) |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram(s) |
| $K_{oc}$ | soil organic carbon-water partition coefficient |
| $K_{ow}$ | *n*-octanol–water partition coefficient |
| L | litre(s) |
| mg | milligram(s) |
| mm | millimetres(s) |
| MOE | margin of exposure |
| mPa | millipascal(s) |
| MRL | maximum residue limit |
| nm | nanometre(s) |
| NAFTA | North American Free Trade Agreement |
| NOAEL | no observed adverse effect level |
| NOEL | no observed effect level |
| OECD | Organisation for Economic Co-operation and Development |
| pH | -log10 hydrogen ion concentration |
| PHED | Pesticide Handlers Exposure Database |
| p*K*a | dissociation constant |
| PMRA | Pest Management Regulatory Agency |
| ppm | parts per million |
| PRVD | Proposed Re-evaluation Decision |
| REI | restricted entry interval |
| TSMP | Toxic Substances Management Policy |
| µg | microgram(s) |
| UV | ultraviolet |
| WDG | water dispersible granule |
| λ | wavelength |

# Appendix I Registered Imazamox Products as of 24 July 2014

| Registration Number | Marketing Class | Registrant | Product Name | Formulation Type | Guarantee |
|---|---|---|---|---|---|
| 25109 | Technical | BASF Canada Inc. | Imazamox Technical Herbicide | Solid | IMZ: 97% |
| 29027 | Manufacturing concentrate | BASF Canada Inc. | Raptor 1AS Bulk | Solution | IMZ: 120 g/L |
| 30506 | Manufacturing concentrate | BASF Canada Inc. | Ares Bulk Herbicide | Solution | IMZ: 33 g/L<br>ARS: 15 g/L |
| 31422 | Manufacturing concentrate | BASF Canada Inc. | Viper ADV Bulk | Solution | BZN: 429 g a.e./L<br>IMZ: 20 g/L |
| 25110 | Commercial | BASF Canada Inc. | AC 299,263 70 WDG | Water dispersible granules | IMZ: 70% a.e. |
| 25111 | Commercial | BASF Canada Inc. | Odyssey WDG Herbicide | Water dispersible granules | IMZ: 35% a.e.<br>IMP: 35% a.e. |
| 25496 | Commercial | BASF Canada Inc. | Solo WDG Herbicide | Wettable granules | IMZ: 70% a.e. |
| 26705 | Commercial | BASF Canada Inc. | AC 299,263 120 AS Herbicide Solution | Solution | IMZ: 120 g/L (present as ammonium salt) |
| 27879 | Commercial | BASF Canada Inc. | Adrenalin SC Herbacide | Emulsifiable concentrate | IMZ: 20 g/L<br>DXF: 560 g a.e. /L |
| 28741 | Commercial | BASF Canada Inc. | Solo WDG Herbicide (Clearfield Crops) | Water dispersible granules | IMZ: 70% a.e. |
| 30188 | Commercial | BASF Canada Inc. | ARES | Solution | IMZ: 33 g/L<br>ARS: 15 g/L |
| 30214 | Commercial | BASF Canada Inc. | Viper A Herbicide (a component of Viper Herbicide tank mix) | Water dispersible granules | IMZ: 70% a.e. |
| 30626 | Commercial | BASF Canada Inc. | Viper ADV | Solution | BZN: 429 g a.e./L<br>IMZ: 20 g/L |
| 31353 | Commercial | BASF Canada Inc. | Odyssey Ultra A (a component of Odyssey Ultra Herbicide Tank Mix) | Water dispersible granules | IMZ: 35% a.e.<br>IMP: 35% a.e. |
| 31504 | Commercial | BASF Canada Inc. | Salute B Herbicide | Solution | IMZ: 33 g/L<br>ARS: 15 g/L |

IMZ – imazamox; ARS – imazapyr; IMP – imazethapyr; DXF – 2,4-D [(2,4-dichlorophenoxy)acetic acid]; BZN – bentazon.

# Appendix II Toxicology Endpoints for Health Risk Assessment for Imazamox

| Exposure Scenario | Dose (mg/kg bw/day) | Study | UF/SF or MOE[1] |
|---|---|---|---|
| Acute dietary | No acute reference dose has been established. | | |
| Chronic dietary | NOEL[2] = 870 | 2-year dietary toxicity study in the rat, no effects observed up to and including the highest dose tested (870 mg/kg bw/day) | 100 |
| | **ADI = 8.7 mg/kg bw/day** | | |
| Short- and intermediate-term dermal | NOEL = 1000 | 28-day dermal toxicity in the rat, no effects observed up to and including the highest dose tested (1000 mg/kg bw/day) | 100 |
| Short- and intermediate-term inhalation[4] | NOAEL[3]= 900 | Developmental toxicity study in the rabbit based on a slightly reduced mean maternal body-weight gain during the dosing and post-dosing periods at the highest dose tested (900 mg/kg bw/day) | 100 |

[1] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to target margin of exposure for occupational or residential assessments.

[2] NOEL refers to no observed effect level.

[3] NOAEL refers to no observed adverse effect level.

[4] An inhalation absorption factor of 100% (default value) is assumed for exposure assessment.

# Appendix III Label Amendments for Products Containing Imazamox

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements provided below.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

I) Under **PRECAUTIONS**, the following statements must be added:

"Do not enter or allow workers entry into treated areas during the restricted entry interval (REI) of 12 hours."

"Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

II) The following statements must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

"TOXIC to non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE."

"To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay."

"Avoid application when heavy rain is forecast."

"Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body."

"The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow."

III) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

"Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground."

**"DO NOT** apply by air."

"As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests."

"DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes."

**Buffer Zones**

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands).

| Method of Application | Crop | Buffer Zones (Metres) Required for the Protection of Terrestrial Habitat |
|---|---|---|
| Field sprayer | Alfalfa, bird's foot trefoil, *Brassica juncea*, canola, dry bean, field pea, lentil, soybeans, sunflower and wheat | 1 |

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners."

The spray drift buffer zones for this product can be modified based on weather conditions and spray equipment configuration by accessing the Buffer Zone Calculator on the Pesticides and Pest Management portion of the Health Canada website.

# References

### Studies/Information Considered in the Chemistry Assessment

### A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT(S)

| PMRA Document Number | Reference |
|---|---|
| 1711748 | 1994, [PRIVACY INFO Removed] 1995-07-20 Series 61-2a, Description of Begining Materials and Manufacturing Process for Technical AC 299,293, DACO: 2.12 |
| 1711801 | 1994, [PRIVACY INFO Removed] 1995-07-20 AC 299,263 Determination of the Melting Point, DACO: 2.16 |
| 1711802 | 1993, [PRIVACY INFO Removed] 1995-07-20 Technical CL 299,263-Color, Physical State, Odor, Bulk Density, Relative Density, pH, Oxidizing/Reducing Properties, DACO: 2.16 |
| 1713819 | 1995, [PRIVACY INFO Removed] 1995-11-01 Screening of CL 299,263 Technical Grade Samples for [CBI Removed], DACO: 2.99 |
| 1714417 | 1996, [PRIVACY INFO Removed] 1996-06-10 CL 299,263 Spectral Database (Report Amendment 2) , DACO: 2.16, 2.99 |
| 1714757 | 1998, [PRIVACY INFO Removed] 1998-03-06 Process Comparison and Equivalency for Imazamox (AC 299,263) Produced in the [CBI Removed], DACO: 2.11.1 |
| 1714761 | 2006, [PRIVACY INFO Removed] 1998-03-06 AC 299,263; CL 299,263; Imazamox; RAPTOR, DACO: 2.13.1,2.13.2,2.13.3,2.13.4 |
| 1714762 | [PRIVACY INFO Removed] 1998-03-06 Chemical and Physical Properties, DACO: 2.14 |
| 1717623 | 1996, [PRIVACY INFO Removed] Screening of Technical Grade CL 299,263 Samples Produced at [CBI Removed], DACO: 2.99 |

### Studies/Information Considered in the Health Assessment

### A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT(S)

| PMRA Document Number | Reference |
|---|---|
| 1160666 | 1995, Metabolism of 14C-CL 299,263 in rats. DACO: 6.4 |
| 1160421 | 1992, Oral $LD_{50}$ study in albino rats with AC299,263 technical; DACO: 4.2.1 |

| PMRA Document Number | Reference |
|---|---|
| 1160422 | 1994, Dermal $LD_{50}$ study in albino rabbits with AC 299,263 technical; DACO: 4.2.2 |
| 1160423 | 1994, Acute inhalation toxicity study with AC 299,263 in rats; DACO: 4.2.3 |
| 1160424 | 1992, Eye irritation study in albino rabbits with AC 299,263 technical; DACO: 4.2.4 |
| 1160425 | 1992, Skin irritation study in albino rabbits with AC 299,263 technical; DACO 4.2.5 |
| 1160426 | 1992, Dermal sensitization study with AC 299,263 in guinea pigs; DACO: 4.2.6 |
| 1160435 | 1995, A 28-day dermal toxicity study with AC 299,263 in rats; DACO: 4.3.4 |
| 1160430 | 1992, A 13-week dietary toxicity study in the albino rat; DACO: 4.3.1 |
| 1160429 | 1994, 90-day dietary toxicity study with AC 299,263 in purebred beagle dogs; DACO: 4.3.1 |
| 1160439 | 1995, One-year dietary toxicity study with AC 299,263 in purebred beagle dogs; DACO: 4.4.1 |
| 1160446/ 1160447 | 1995, An oncogenicity study with AC 299,263 in mice; DACO; 4.4.2 |
| 1160437/ 1160438 | 1995, Chronic dietary toxicity and oncogenicity study with AC 299,263 in the albino rat; DACO: 4.4.1, 4.4.2 |
| 1160445 | 1994, Evaluation of CL 299,263 in a bacterial/microsome mutagenicity assay; DACO: 4.5.4 |
| 1160444 | 1993, Evaluation of CL 299,263 in the mammalian cell CHO/HGPRT mutagenicity assay; DACO: 4.5.4 |
| 1160469 | 1994, Test for chemical induction of chromosome aberration in cultured Chinese hamster ovary (CHO) cells with and without metabolic activation; DACO: 4.5.4 |
| 1160458 | 1993, In vivo micronucleus assay in mouse bone marrow cells; DACO: 4.5.4 |
| 1160441 | 1995, A two-generation reproduction study with AC 299,263 in rats; DACO: 4.5.1 |
| 1160442 | 1994, An oral developmental toxicity (embryo-fetal toxicity/teratogenicity) study with AC 299,263 in rats; DACO: 4.5.2 |
| 1160443 | 1995, An oral developmental toxicity (embryo-fetal toxicity/teratogenicity) definitive study with AC 299,263 in rabbits; DACO: 4.5.2 |
| 2115788 | 2008, Agricultural Reentry Task Force (ARTF). Data Submitted by the ARTF to Support Revision of Agricultural Transfer Coefficients, Submission #2006-0257; DACO: 5.1. |

## Studies/Information Considered in the Environmental Assessment

## A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT(S)

| PMRA Document Number | Reference |
|---|---|
| 1160623 | 1995, Aqueous photolysis of AC 299,263, DACO: 8.2.1 |
| 1160628 | 1995, Biotransformation of 14C-AC 299,263 under aerobic aquatic conditions. Final report, DACO: 8.2.3.1 |
| 1160668 | 1995, Pilot dietary toxicity study with AC 299,263 technical in mallard duck (*Anas platyrhynchos*), DACO: 9.6.3.1. |
| 1160669 | 1995, Pilot dietary toxicity study with AC 299,263 technical in northern bobwhite (*Colinus virginianus*), DACO: 9.6.3.1 |
| 1160759 | 1995, Effect of AC 299,263 on Non-target Emerged Aquatic Plants, DACO: 9.8.5 |
| 1160629 | 1995, Biotransformation of 14C-AC 299,263 under anaerobic aquatic conditions. Final report, DACO: 8.2.3.1 |
| 1160686 | 1994, 14-day acute toxicity test with AC 299,263 technical in mallard duck (*Anas platyrhynchos*), DACO: 9.6.2.1 |
| 1160688 | 1994, 14-day acute toxicity test with AC 299,263 technical in northern bobwhite (*Colinus virginianus*), DACO: 9.6.2.1 |
| 1160687 | 1994, 8-day acute dietary test with AC 299,263 technical in mallard duck (*Anas platyrhynchos*), DACO: 9.6.2.1 |
| 1160667 | 1994, 8-day acute dietary test with AC 299,263 technical in northern bobwhite (*Colinus virginianus*), DACO: 9.6.2.1 |
| 1162817 | 1995, Metabolism of carbon-14 labeled CL 299,263 in peas under field conditions, DACO: 6.3 |
| 1160620 | 1995, Hydrolysis of AC 312,622, DACO: 8.2.1 |
| 1160679 | 1995, 14-day acute toxicity study with AC 299,263 in the earthworm (*Eisenia foetida*). Final report, DACO: 9.2.3.1 |
| 1160677 | 1994, Confined accumulation study of carbon-14 labeled CL 299,263 using radishes, corn, lettuce, and wheat as rotational crops, DACO: 6.3 |
| 1160670 | 1995, Reproduction study with AC 299,263 technical in the mallard ducks (*Anas platyrhynchos*), DACO: 9.6.3.1 |
| 1160671 | 1995, Reproduction study with AC299,263 technical in the northern bobwhite (*Colinus virginianus*), DACO: 9.6.3.1 |
| 1160762 | 1995, Effect of AC 299,263 on the growth of *Lemna gibba* (duckweed), DACO: 9.8.5 |

| PMRA Document Number | Reference |
|---|---|
| 1160689 | 1995, Effect of AC 299,263 on the growth of *Anabaena flos-aquae*, DACO 9.8.2 |
| 1160700 | 1995, Effect of AC 299,263 on the growth of *Navicula pelliculosa*, DACO: 9.8.2 |
| 1160711 | 1995, Effect of AC 299,263 on the growth of *Selenastrum capricornutum*, DACO: 9.8.2 |
| 1160736 | 1995, Effect of AC 299,263 on the growth of *Skeletonema costatum*, DACO: 9.8.3 |
| 1160675 | 1995, Uptake, depuration, bioconcentration and metabolism of [14C]-c l299,263 in Bluegill sunfish (*Lepomis macrochirus*) under flow-through test conditions, DACO: 9.5.5 |
| 1160653 | 1995, Soil rate of dissipation study with CL 299,263 70DG in Alberta, Canada, DACO: 8.3.2.3 |
| 1160652 | 1995, Soil rate of dissipation study with CL 299,263 70DG in Alberta, Canada, DACO: 8.3.2.3 |
| 1160654 | 1995, Soil rate of dissipation study with CL 299,263 70DG in Saskatchewan, Canada, DACO: 8.3.2.3 |
| 1160656 | 1995, Soil rate of dissipation study with CL 299,263 70DG in Manitoba, Canada, DACO: 8.3.2.3 |
| 1161119 | 1995, Soil rate of dissipation study with CL 299,263 in Ontario Canada, DACO: 8.3.2.3 |
| 1161120 | 1995, Soil rate of dissipation study with CL 299,263 in Ontario Canada, DACO: 8.3.2.3 |
| 1160627 | 1995, Biotransformation of 14C-AC 299,263 under aerobic soil conditions. Final report, DACO: 8.2.3.1 |
| 1160660 | 1994, Metabolism of carbon-14 labeled CL 299,263 in soybean under field conditions, DACO: 6.3 |
| 1160619 | 1994, Hydrolysis, DACO: 8.2.1 |
| 1160625 | 1994, Adsorption/desorption, DACO: 8.2.4.1 |
| 1160626 | 1995, Determination of the mobility of AC 299,263 and its soil metabolite (CL312,622) by soil TLC, DACO: 8.2.4.1 |
| 1160682 | 1995, Metabolism of carbon-14 labeled CL 299,263 in field grown canola, DACO: 6.3 |
| 1160624 | 1994, Determination of the n-Octanol/Water partition coefficient, DACO: 8.2.2.1 |

| PMRA Document Number | Reference |
|---|---|
| 1189719 | 1994, An acute contact toxicity study with AC 299,263 in the honey bee (*Apis mellifera* L.), DACO: 9.2.4.1 |
| 1166131 | 1996, The effects of AC 299,263 on the respiration and nitrification of soil microflora, DACO: 9.2.7 |
| 1160621 | 1995, Photodegradation on soil, DACO: 8.2.1 |
| 1160674 | 1995, Acute toxicity of AC 299,263 to the Rainbow trout (*Oncorhynchus mykiss*) under flow-through test conditions, DACO: 9.5.2.1 |
| 1160680 | 1994, Acute toxicity of AC 299,263 to *Daphnia magna* under flow-through test conditions, DACO: 9.3.1 |
| 1160673 | 1994, Acute toxicity of AC 299,263 to the Bluegill sunfish (*Lepomis macrochirus*) under flow-through test conditions, DACO: 9.5.2.1 |
| 1165765 | 1995, Final report: Chronic toxicity of AC 299,263 during the complete life-cycle of *Daphnia magna* under flow-through test conditions, DACO: 9.3.3 |
| 1165761 | 1995, Toxicity of AC299,263 to the Rainbow trout (*Oncorhynchus mykiss*) after 28 days of exposure under flow-through test conditions, DACO: 9.5.2.1 |