Proposed Registration Decision PRD2018-03

Flazasulfuron and Flazasulfuron 25WG Herbicide

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Overview

Proposed Registration Decision for Flazasulfuron

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 Technical Flazasulfuron Herbicide and Flazasulfuron 25WG Herbicide, containing the technical grade active ingredient flazasulfuron, for pre- and postemergent control or suppression of grasses, broadleaf weeds and sedges in grapes, conifer trees and industrial vegetation management sites.

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 Technical Flazasulfuron Herbicide and Flazasulfuron 25WG 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.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides.

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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."

For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Canada.ca at https://www.canada.ca/en/health-canada/services/consumer-product-safety/pesticides-pest-management.html.

Before making a final registration decision on flazasulfuron, the PMRA will consider any comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on flazasulfuron, 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 Flazasulfuron?

Flazasulfuron is a herbicide that inhibits production of branched-chain amino acids required for protein synthesis in plants. This results in the cessation of cell division and plant growth. Susceptible plants die shortly after exposure to sunlight. Flazasulfuron can be absorbed through both the roots and foliage of the plants.

Health Considerations

Can Approved Uses of Flazasulfuron Affect Human Health?

Flazasulfuron 25WG Herbicide, containing flazasulfuron, is unlikely to affect human health when used according to label directions.

Potential exposure to flazasulfuron may occur through the diet (food and water) or when handling and applying the end-use product Flazasulfuron 25WG Herbicide. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

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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*.

In laboratory animals, flazasulfuron and the end-use product, Flazasulfuron 25WG Herbicide, were of low acute toxicity by the oral, dermal, and inhalation routes of exposure. They were not irritating to the skin and were minimally irritating to the eye. They did not cause an allergic skin reaction.

Registrant-supplied short- and long-term (lifetime) animal toxicity tests were assessed for the potential of flazasulfuron to cause neurotoxicity, immunotoxicity, chronic toxicity, cancer, reproductive and developmental toxicity, and various other effects. There was no evidence that the young were more sensitive than the adult animal. The most sensitive endpoints for risk assessment were effects noted in the liver and kidneys. The risk assessment protects against the effects of flazasulfuron 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 drinking water are not of health concern.

Aggregate dietary intake estimates (food plus drinking water) revealed that the general population and infants less than one year old, the subpopulation which would ingest the most flazasulfuron relative to body weight, are expected to be exposed to less than 64% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from flazasulfuron is not of health concern for all population subgroups.

Acute dietary (food plus drinking water) intake estimates for the general population and all population subgroups were less than 4% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was all infants less than one year old.

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

Residue trials conducted throughout the United States using flazasulfuron on grapes are acceptable. The MRL for this active ingredient can be found in the Science Evaluation of this consultation document.

Occupational Risks From Handling Flazasulfuron 25WG Herbicide

Occupational risks are not of concern when Flazasulfuron 25WG Herbicide is used according to the label directions, which include mitigation measures.

Workers mixing, loading, and applying Flazasulfuron 25WG Herbicide, and workers re-entering recently treated non-cropland areas can come in direct contact with Flazasulfuron 25WG Herbicide residues on the skin. Therefore, the label specifies that during mixing, loading, clean up and repair, handlers must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes plus socks, and protective eyewear. During application, workers must wear a long-sleeved shirt, long pants, chemical-resistant gloves (not required inside closed-cab equipment), and shoes plus socks.

When using groundboom equipment and handling more than 48 kg Flazasulfuron 25WG Herbicide in a day, in addition to wearing the personal protective equipment listed above, mixers and loaders must wear chemical-resistant coveralls and chemical-resistant footwear.

The label also requires that workers do not enter or be allowed entry into treated vineyards, conifer trees (field- and container-grown), and conifer release (forestry) areas, during the restricted-entry interval (REI) of 12 hours; and do not enter or allow others to enter treated non-cropland or industrial vegetation areas until sprays have dried. Taking into consideration these label statements and the expectation of the exposure durations for handlers and postapplication workers, the risks to these individuals are not of concern.

Bystanders are not expected to be in a treatment area during application. A standard label statement to protect against drift during application is on the label. Health risks are not of concern for bystanders entering treated industrial vegetation and conifers on the day of application.

Environmental Considerations

What Happens When Flazasulfuron Is Introduced Into the Environment?

When used according to label directions, flazasulfuron is not expected to pose risks of concern to the environment.

Flazasulfuron can enter the environment when applied to control weeds in grapes, in conifer trees, forests, and in industrial sites. It does not, however, remain in the environment for a long time. It breaks down by reacting with water to form several breakdown products. Flazasulfuron is not expected to move into the air from water or moist soils. It is not expected to accumulate in the tissues of organisms. It is not expected to carry over into the next growing season. Flazasulfuron and its breakdown products have the potential to move through soil to reach groundwater and run-off into surface water. A precautionary label statement is required to inform users that flazasulfuron can reach groundwater. Specific instructions are required to minimize risk of runoff from treated areas into aquatic habitats.

Flazasulfuron and its breakdown products do not present a risk of concern to birds, small wild mammals, bees, fish, amphibians, beneficial arthropods (such as beetle and spider), and invertebrates (such as earthworms and water fleas). Flazasulfuron and its breakdown products may affect non-target plants on land and in the water from spray drift and run-off. To minimize exposure and reduce risks to non-target plants, spray buffer zones and precautionary label statements are required.

Value Considerations

What Is the Value of Flazasulfuron 25WG Herbicide?

Flazasulfuron 25WG Herbicide provides pre- and postemergent control or suppression of grasses, broadleaf weeds, and sedges in grapes and conifer trees and for industrial vegetation management.

Flazasulfuron 25WG Herbicide provides pre- and postemergent control of grasses, broadleaf weeds, and sedges, with residual activity and tank-mix flexibility. It controls key weeds which are present in agricultural and forestry systems, including ragweed, pigweed, nightshade, and lamb's-quarters. Control of broadleaf weeds with flazasulfuron in Christmas trees has been identified as a priority by Canadian growers.

The registration of Flazasulfuron 25WG Herbicide would provide Canadian growers not only with access to a product that is currently available in the United States for the same uses, but also a new mode of action for managing weeds in grapes and conifer trees. Flazasulfuron 25WG Herbicide may be particularly useful in managing weeds that have developed resistance to other modes of action.

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 Flazasulfuron 25WG Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

To reduce the potential of workers coming into direct contact with Flazasulfuron 25WG Herbicide on the skin or through inhalation of sprays, workers must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes plus socks, and goggles or face shield during mixing, loading, clean-up and repair. During application, workers must wear a long-sleeved shirt, long pants, chemical-resistant gloves (not required inside closed-cab equipment), and shoes plus socks.

When using groundboom equipment and handling more than 48 kg Flazasulfuron 25WG Herbicide in a day, in addition to wearing the personal protective equipment listed above, mixers and loaders must wear chemical-resistant coveralls and chemical-resistant footwear.

The label also requires that workers do not enter or be allowed entry into treated vineyards and conifer trees (field- and container-grown), and conifer release (forestry) areas, during the REI of 12 hours; and do not enter or allow others to enter treated non-cropland or industrial and vegetation areas until sprays have dried.

Environment

Precautionary label statements are required to inform users of the potential risks of flazasulfuron to groundwater. Specific instructions are required to minimize risk of runoff from treated areas into aquatic habitats. To minimize exposure and reduce risks to plants in water and land, spray buffer zones and precautionary label statements are required.

Next Steps

Before making a final registration decision on flazasulfuron, the PMRA will consider any 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

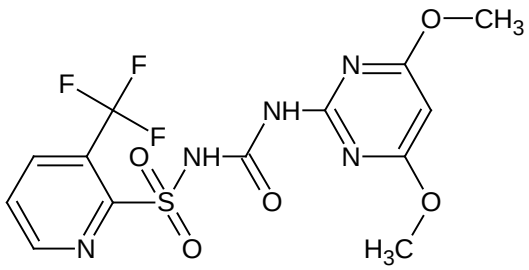
When the PMRA makes its registration decision, it will publish a Registration Decision on flazasulfuron (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the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

Science Evaluation

Flazasulfuron

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Flazasulfuron
Function	Herbicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	N-[(4,6-dimethoxypyrimidin-2-yl)carbamoyl]-3-(trifluoromethyl)pyridine-2-sulfonamide
2. Chemical Abstracts Service (CAS)	N-[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]-3-(trifluoromethyl)-2-pyridinesulfonamide
CAS number	104040-78-0
Molecular formula	$C_{13}H_{12}F_3N_5O_5S$
Molecular weight	407.36
Structural formula	
Purity of the active ingredient	99.4 %

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

Technical Product—Technical Flazasulfuron Herbicide

Property	Result
Colour and physical state	cream coloured granular solid
Odour	strong lawn fertilizer odour
Melting range	147–150°C

Property	Result
Boiling point or range	Not applicable
Density	0.66 g/cm^3 (bulk density)
Vapour pressure at 20°C	$<1.33 \times 10^{-5}$ Pa
Henry's law constant at 20°C	2.55×10^{-11} Pa·m^3·mol^{-1}
Ultraviolet (UV)-visible spectrum	pH / λ_{max} (nm) / ε (L/(mol cm)) 4 / <250 / <500 (at 250nm) 5 / 251 / 737 7 / 251 / 6747 9 / 251 / 14521
Solubility in water at 25°C	pH 5 buffer: 0.027 g/L pH 7 buffer: 2.1 g/L
Solubility in organic solvents at 25°C	Solvent / Solubility (mg/mL) hexanes / 0.00050 octanol / 0.20 toluene / 0.56 methanol / 4.2 ethyl acetate / 6.9 acetonitrile / 8.7 dichloromethane / 22.1 acetone / 22.7
n-Octanol-water partition coefficient (K_{ow})	pH / log K_{ow} 5 / 1.30 7 / -0.06
Dissociation constant (pK_a)	pK_a = 4.37
Stability (temperature, metal)	Unstable at elevated temperatures when exposed to air. Moderately sensitive to metals and their salts at elevated temperatures. Stable at elevated temperatures when protected from air.

End-Use Product—Flazasulfuron 25WG Herbicide

Property	Result
Colour	grey brown
Odour	cinnamon-like
Physical state	granular solid
Formulation type	water dispersible granules
Guarantee	25 %
Container material and description	Plastic bottle or drum
Density	0.7–0.9 g/cm^3
pH of 1% dispersion in water	4–6 (1 % suspension in water)

Property	Result
Oxidizing or reducing action	Not an oxidizer, expected to react with strong oxidizers
Storage stability	Stable at ambient temperatures for at least one year
Corrosion characteristics	Not corrosive to plastic packaging material
Explodability	Not expected to be explosive

1.3 Directions for Use

Pre- and postemergent applications of Flazasulfuron 25WG Herbicide at a rate range of 150-200 g/ha provide control or suppression of grasses, broadleaf weeds, and sedges in grapes and conifer trees and for industrial vegetation management. The higher rate is for control or suppression of larger weeds and heavier infestations.

For postemergent application, Flazasulfuron 25WG Herbicide is recommended for application with a non-ionic surfactant (NIS) at 0.25% v/v or a Crop Oil Concentrate (COC) or Methylated Seed Oil (MSO) at 1.0% v/v.

For improved burndown weed control, Flazasulfuron 25WG Herbicide is recommended for application in tank-mix with glyphosate or glufosinate-ammonium herbicides, which are labelled for the same use pattern and timing on the same crop.

For longer residual weed control, Flazasulfuron 25WG Herbicide is recommended for application in tank-mix with diuron- and simazine- containing herbicides.

Grapes: Flazasulfuron 25WG may be applied as a directed spray to grape vines established for at least three years. Use of a protective sleeve is required for the third year vines to minimize injury potential. Do not apply to areas where roots are exposed or suckers are actively growing and have not hardened off.

Conifer Trees: Flazasulfuron 25WG may be applied over-the-top to conifers, which are established for more than a year, prior to spring bud break or when conifers are sufficiently hardened off. Directed applications are recommended to reduce injury potential as well as for conifers that have new growth or are not sufficiently hardened off.

Industrial Vegetation Management: Flazasulfuron 25WG may be applied after weeds break dormancy. Best results can be obtained if weeds are small or one to two weeks after mowing.

1.4 Mode of Action

The active ingredient flazasulfuron formulated in Flazasulfuron 25WG is a sulfonylurea herbicide which acts by inhibiting acetolactate synthase (ALS), a key enzyme for branched-chain amino acid synthesis. This results in the cessation of cell division and plant growth. Susceptible plants become necrotic and die shortly after exposure to sunlight. Flazasulfuron can be absorbed through both the roots and foliage of the plants.

Flazasulfuron is classified as a Group 2 herbicide by the Weed Science Society of America and as a Group B herbicide by the Herbicide Resistance Action Committee.

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 impurities in the technical product 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

High-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes in soil/sediment and water. A high-performance liquid chromatography method with ultraviolet spectrometry detection was provided for animal biota. 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.

An HPLC-MS/MS method (Method S09-03106) was developed and proposed for data generation and enforcement purposes in plant matrices. The method fulfilled the requirements with regards to specificity, accuracy and precision at the method limit of quantitation. Acceptable recoveries (70–120%) were obtained in plant matrices. The proposed enforcement method was successfully validated in plant matrices (olive, wheat and tomatoes) by an independent laboratory. Extraction solvents used in the method were similar to those used in the metabolism studies; thus, further demonstration of extraction efficiency with radiolabelled crops was not required for the enforcement method.

Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicology database for flazasulfuron, also known as SL-160, was conducted. The database consists of the full array of toxicity studies currently required for health hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is acceptable. The database is considered adequate to define the majority of toxic effects that may result from exposure to flazasulfuron.

Metabolism and toxicokinetics in the rat were investigated using radiolabelled flazasulfuron (^{14}C-pyridine -SL-160 and ^{14}C-pyrimidine-SL-160) in single low and high dose, as well as repeated low dose oral gavage studies. Flazasulfuron was rapidly and well absorbed with peak plasma concentrations (C_{max}) reached in both sexes within 0.5 hours and 4-6 hours at the low- and high-dose, respectively. By 48 hours post-exposure, males and females absorbed 93-99% of the low-dose and 84-93% of the high-dose. At 168 hours, the blood concentrations decreased to less than 1.7% of C_{max}. The absorbed radiolabel was distributed mainly to the blood, liver, muscle, carcass, and bone. Elimination of orally-administered flazasulfuron was rapid and extensive. Almost all administered dose (AD) was recovered in the excreta within 72 hours. Urine was the major route of excretion. Radioactivity in tissues after single or repeat oral dose administration was low, <4% AD in males and <1% AD in females. Urinary excretion in females was greater than in males, whereas fecal elimination in males was greater than in females. This sex difference in the route of elimination was independent of dose levels. The distribution and excretion of radiolabel following pretreatment of multiple non-radiolabeled doses was not significantly different from that following administration of a single radiolabeled dose.

Metabolism of flazasulfuron in the rat included molecular rearrangement, cleavage at the sulfonylurea bridges, oxidation, displacement, and glucuronic acid conjugation. Unchanged flazasulfuron accounted for the majority of radioactivity in urine, with lesser amounts in feces and bile. The major metabolites in the urine and feces were identified as HDTG+TPPG. Minor urinary and fecal metabolites were HDPU, HTPP, and DTPU. TPSA and MTMG were minor urinary metabolites, and HDU and ADMP were identified in the feces. See Appendix I, Table 2 for identification of metabolites.

The acute toxicity of flazasulfuron was low by the oral, dermal, and inhalation routes of exposure in rats. Flazasulfuron was non-irritating to the skin and minimally irritating to the eyes of rabbits. It was not a skin sensitizer based on the results of the dermal sensitization test using the Buehler's test protocol in guinea pigs.

Flazasulfuron 25WG Herbicide was of low acute toxicity by the oral, dermal, and inhalation routes of exposure in rats. It was not a skin irritant in rabbits, and was minimally irritating to the eye in rabbits. It was not a skin sensitizer in guinea pigs based on the results of sensitization testing using the Buehler's method.

No systemic toxicity or localized skin effects occurred in rabbits following daily dermal application of the limit dose of flazasulfuron for 21 days.

In repeated-dose gavage/dietary toxicity studies in mice, rats, and dogs, the liver was the main target organ. At high dose levels, administration of flazasulfuron resulted in lower body weights and body weight gains, and pathology of the liver (increased brown pigment, inflammatory cell infiltration). In the rat, kidney pathology (focal tubular atrophy and dilatation of proximal tubules) was also observed and the lesions increased in severity with duration of treatment. The mechanism of kidney pathology was investigated in a 2-week study in rats, but the findings were inconclusive. There was no evidence of oncogenic potential of flazasulfuron.

Flazasulfuron was tested for potential genotoxic activity in a standard battery of in vitro and in vivo assays. Based on the uniformly negative results of these studies, flazasulfuron was not genotoxic.

A dietary reproductive toxicity study in rats did not demonstrate reproductive toxicity or evidence of sensitivity of the young. In addition to kidney toxicity in parental animals, high dose levels caused lower body weight gain of the parents and offspring.

Developmental toxicity studies were conducted in rats and rabbits via oral gavage. The high dose level in the rat study resulted in reduced food consumption and body weight of the dams and reduced weight and delayed skeletal ossification in fetuses. In the rabbit study, the highest dose level resulted in abortions after the end of the dosing period, which were preceded by significant reduction in food intake and body weight of the dams. There was no evidence of sensitivity of the fetus.

There were no gross or histopathological changes in the central or peripheral nervous system following either acute gavage or short-term dietary exposure to flazasulfuron in the rat. Transient reduction in motor activity was observed at a high dose level in the acute neurotoxicity study. No treatment-related findings were observed in the short-term neurotoxicity study at lower dose levels.

An immunotoxicity study in female mice demonstrated that flazasulfuron did not affect the weight of the spleen, spleen cellularity, or specific activity and total spleen activity, as measured by the antibody-forming cell assay.

Results of the toxicology studies conducted on laboratory animals with flazasulfuron and its end-use product are summarized in Appendix I, Tables 3 and 4. The toxicology reference values for use in the human health risk assessment are summarized in Appendix I, Table 5.

Incident Reports

Flazasulfuron is a new active ingredient pending registration for use in Canada, and there are currently no incident reports. Once products containing flazasulfuron are registered, the PMRA will monitor for incident reports.

3.1.1 *Pest Control Products Act* Hazard Characterization

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

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database contained the standard complement of required studies including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in the rat.

With respect to potential prenatal and postnatal toxicity, there was no indication of increased sensitivity of the young animal compared to the parental animal in the reproductive and developmental toxicity studies. In the reproductive toxicity study, at a maternally toxic dose level, there was a reduction of birth and pup weights. Developmental toxicity was demonstrated in the rat in the form of delayed fetal ossification and decreased fetal body weight occurring in the presence of maternal toxicity. In the rabbit developmental toxicity study, an increased incidence of abortions occurred following the cessation of dosing in high-dose dams; this dose level was associated with significant reduction in food intake and body weight of the dams.

Overall, the database is adequate for determining the sensitivity of the young. The abortions in the rabbit were considered a serious endpoint although the level of concern was tempered by the fact that they occurred in the presence of overt toxicity in the dams. Therefore, the *Pest Control Products Act* factor was reduced to 3-fold when using this endpoint from the rabbit developmental toxicity study to establish the point of departure for risk assessment. The *Pest Control Products Act* factor was reduced to 1-fold for all other scenarios.

3.2 Determination of Acute Reference Dose

To estimate risk from a single dietary exposure, the acute neurotoxicity study in the rat with a no observed adverse effect level (NOAEL) of 50 mg/kg bw was selected. At the lowest observed adverse effect level (LOAEL) of 1000 mg/kg bw, a transient decrease in motor activity was evident. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. The composite assessment factor (CAF) is thus 100.

The acute reference dose (ARfD) is calculated according to the following formula:

$$\text{ARfD} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{50\,\text{mg/kg bw}}{100} = 0.5\,\text{mg/kg bw}$$

3.3 Determination of Acceptable Daily Intake

To estimate risk from repeat dietary exposure, the 2-year dietary toxicity study in the rat with a NOAEL of 1.3 mg/kg bw/day was selected. At the LOAEL of 13.3 mg/kg bw/day, chronic nephropathy was observed. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. As discussed in the *Pest Control Products Act* Hazard Characterization section, the *Pest Control Products Act* factor was reduced to 1-fold. The CAF is thus 100.

The acceptable daily intake (ADI) is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{CAF}} = \frac{1.3\,\text{mg/kg bw/day}}{100} = 0.01\,\text{mg/kg bw/day}$$

The ADI provides a margin of 15,000 to the NOAEL for abortion in the rabbit developmental toxicity study and is considered protective for pregnant women and their unborn children.

Cancer Risk Assessment

There was no evidence of carcinogenicity; therefore, a cancer risk assessment was not required.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Occupational exposures to Flazasulfuron 25WG Herbicide are characterized as mainly via the dermal and inhalation routes for mixers, loaders and applicators, and through the dermal route for postapplication re-entry workers and bystanders. Treatments of grapes and conifers are expected to be of short-term duration, as they are conducted by farmers/operators, and short-term duration for postapplication exposures. Treatments and postapplication tasks for vegetation management are expected to be of intermediate-term duration for custom/commercial workers who are likely to apply the product and return to many sites throughout several months (up to 6 months) of the weed control season.

Short-term Dermal and Inhalation Exposure

For short-term exposure via the dermal and inhalation routes, the acute oral neurotoxicity study in the rat was selected for risk assessment. An oral study was selected since the available repeat-dose dermal toxicity study did not assess the endpoint of concern, namely decreased motor activity, and a repeat-dose inhalation toxicity study was not available. A NOAEL of 50 mg/kg bw was established in the acute neurotoxicity study. At the LOAEL of 1000 mg/kg bw, there was a transient decrease in motor activity. The target margin of exposure (MOE) selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. The rabbit developmental toxicity study was also given consideration, however, the selection of the acute neurotoxicity endpoint and target MOE provides an adequate margin to the serious endpoint of abortions in this study. 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.

Intermediate-term Dermal and Inhalation Exposure

For intermediate-term exposure via the dermal and inhalation routes, the 90-day dog oral toxicity study with a NOAEL of 2 mg/kg bw/day was selected for risk assessment. At the LOAEL of 10 mg/kg bw/day, liver pathology was observed. An oral study was selected since the available repeat-dose dermal toxicity study did not assess the endpoint of concern, namely abortions in the rabbit developmental toxicity study, and a repeat-dose inhalation toxicity study was not available. The target MOE selected for this endpoint is 100. Ten-fold factors were applied each for interspecies extrapolation and intraspecies variability. The selection of this endpoint and target MOE provides an adequate margin to the abortions in the rabbit developmental toxicity study and is considered to be protective of all populations, including nursing infants and the unborn children of exposed female workers.

Cumulative Risk Assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. For the current evaluation, the PMRA did not identify information indicating that flazasulfuron shares a common mechanism of toxicity with other pest control products. Therefore there is no requirement for a cumulative assessment at this time.

3.4.1.1 Dermal Absorption

A product-specific dermal absorption study was not submitted. Therefore, the default dermal absorption value of 100% was used.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/Loader/Applicator Exposure and Risk Assessment

Individuals have potential for exposure to Flazasulfuron 25WG Herbicide during mixing, loading, and application. Dermal and inhalation exposure estimates of workers were generated using the Pesticide Handlers Exposure Database (PHED v.1.1, 2002) and the Agricultural Handlers Exposure Task Force (AHETF) database (Table 3.4.2.1-1).

Exposure estimates were derived for mixers, loaders, and applicators applying Flazasulfuron 25WG Herbicide to vineyards, industrial vegetation, and conifer trees (container- and field-grown trees, or conifer release (forestry)). Exposures are estimated for workers wearing a long-sleeved shirt, long pants, chemical-resistant gloves, and shoes plus socks during mixing, loading, application, clean-up and repair.

Chemical-specific data for assessing human exposures during pesticide handling activities were not submitted.

Exposures were estimated by coupling the dermal and inhalation unit exposure values from the PHED or AHETF databases with the dermal absorption value of 100% and inhalation systemic absorption of 100%, and the amount of product handled per day. Exposures were normalized to mg/kg bw/day by using 80 kg as the adult body weight.

Combined dermal and inhalation exposures were compared to an oral toxicological endpoint NOAEL to obtain the MOE. The target MOE is 100 for dermal and inhalation routes (Table 3.4.2.1-2).

Table 3.4.2.1-1 Mixer, Loader, and Applicator Unit Exposures for workers handling Flazasulfuron 25WG Herbicide

Scenario		Unit Exposure (µg/kg a.i. handled)		Personal Protective Equipment
		Dermal	Inhalation [a]	
A	Open M/L Dry Flowable, (AHETF)	84.14	21.8	single layer + gloves
B	Open M/L, Dry Flowable (AHETF)	39.13	21.8	chemical-resistant coveralls + single layer + gloves
C	Applicator, open cab groundboom (AHETF)	25.4	1.68	single layer + gloves
D	Applicator, open cab airblast (AHETF)	3769.3	9.08	single layer + gloves
E	Applicator, Right-of-Way sprayer (PHED)	872.54	5	single layer + gloves
F	M/L/A backpack (liquid) (PHED)	5445.85	62.1	single layer + gloves
G	M/L/A Mechanically-pressurized handgun (liquid) (PHED)	5585.49	151	single layer + gloves

Note: single layer + gloves mean a long-sleeved shirt and long pants plus chemical-resistant gloves;
M/L = mixer/loader, M/LA = mixer/loader and applicator

a. Light inhalation; except moderate inhalation rate used for backpack

Table 3.4.2.1-2 Mixer, loader, and applicator exposure and risk estimates of handling Flazasulfuron 25WG Herbicide

PPE Scenario [a]	Scenario	Amount of a.i. handled per day [b] (kg a.i./day)	Unit Exposure (µg/kg a.i. handled)		Exposure [c] (mg/kg bw/day)		Dermal + Inhalation	
			Dermal	Inhalation	Dermal	Inhalation	Short-term MOE [d] (target=100)	Intermediate-term MOE [d] (target=100)
M/L + groundboom								
A+C	M/L (open)/A (open cab)	1.3	109.54	23.48	0.00178	0.000382	23127	------

Table 3.4.2.1-2 Mixer, loader, and applicator exposure and risk estimates of handling Flazasulfuron 25WG Herbicide

PPE Scenario [a]	Scenario	Amount of a.i. handled per day [b] (kg a.i./day)	Unit Exposure (µg/kg a.i. handled)		Exposure [c] (mg/kg bw/day)		Dermal + Inhalation	
			Dermal	Inhalation	Dermal	Inhalation	Short-term MOE [d] (target=100)	Intermediate-term MOE [d] (target=100)
M/L + groundboom								
A+C	M/L (open)/A (open cab)	5.35	109.54	23.48	0.00733	0.001570	5618	------
A+C	M/L (open)/A (open cab)	12 [e]	109.54	23.48	0.01643	0.003522	2506	100
B+C	M/L (open)/A (open cab)	18 [f]	64.53	23.48	0.01452	0.005283	2525	101

M/L + airblast								
A+D	M/L (open)/A (open cab)	1	3853.44	30.88	0.04817	0.000386	1030	-----
M/L + Rights-of-Way sprayer								
A+E	M/L (open)/A (open cab)	1.27	956.68	26.8	0.01519	0.000425	3202	128
Backpack equipment (covers manually-pressurized handwand, if used)								
A+F	M/L/A	0.02	5529.99	83.9	0.00138	0.000021	35689	1428
Mechanically-pressurized handgun								
A+G	M/L/A	1.27	5669.63	172.8	0.09001	0.002743	539	-----

a. From Table 3.4.2.1-1;
b. Amount of ai handled per day = maximum application rate × ATPD
Groundboom: 26 ha/day for vineyard; 107 ha/day for ornamental and Christmas conifers; 360ha/day for conifer release and industrial vegetation management;
Airblast: 20 ha/day for conifer release
Right-of-Way and mechanically-pressurized handgun: 3800 L/day default volume per day ÷ (min. 150 L spray volume/ha);
Backpack: 150 L/day default volume per day × 0.5 g product (0.125 g a.i.) /L;
c. Exposure (mg/kg bw/day; dermal and inhalation) = Amount of ai handled per day × unit exposure × absorption / body weight
Where, dermal absorption - 100%; inhalation absorption - 100%
body weight (adult), = 80 kg
d. Margin of Exposure (MOE) = NOAEL / Exposure (dermal + inhalation)
Where, NOAEL (oral) = 50 mg/kg bw for short-term duration exposures; 2 mg/kg bw/day for intermediate-term duration exposures;
e. Maximum amount of active ingredient that can be handled per day (48 kg product/day) when a worker wears a single layer of personal protective equipment and chemical-resistant gloves;
f. When handling more than 12 kg a.i./day (48 kg product), mixers and loaders must wear chemical-resistant coveralls and chemical-resistant footwear in additional to a single layer of personal protective equipment plus chemical-resistant gloves.

Risks of concern for mixers, loaders, and applicators are not expected when label precautions are followed which include wearing a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes.

However, when using groundboom equipment and handling more than 48 kg Flazasulfuron 25WG Herbicide in a day, in addition to wearing the personal protective equipment listed above, mixers and loaders must wear chemical-resistant coveralls and chemical-resistant footwear.

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure of workers re-entering areas treated with Flazasulfuron 25WG Herbicide. However, worker exposures to treated soil (vineyard pre- and post-emergence applications to weeds) and bare-ground (pre-emergence applications in industrial vegetation and in conifers) are considered minimal, as workers will be wearing personal protective equipment appropriate to the use scenario tasks. Therefore, no postapplication risk assessment is conducted for these sites.

After post-emergence applications, workers are exposed when re-entering treated industrial vegetation and non-cropland areas, conifer trees and forestry lands to conduct site-specific activities such as scouting, or other forestry-related tasks. Scouting in treated industrial vegetation and non-cropland areas are not expected to be as intense as other forestry related tasks. No information was provided to estimate exposure to military personnel, but since the non-military sites represent the same treatments (e.g. airports, ditch banks, dry canals, railroad and utility rights-of-way, roadsides, industrial sites, manufacturing sites, storage areas and warehouse areas), exposures are expected to be representative for military personnel also.

Chemical-specific dislodgeable foliar residue data were not submitted. Therefore, risk assessments were conducted using the default dislodgeable foliar residue (DFR) value of 25% of the application rate on the day of application, and thereafter the default daily dissipation rate of 10%, with transfer coefficients from the Agricultural Re-entry Task Force (ARTF) database, 100% dermal absorption, exposure time, and adult body weight (Table 3.4.2.2-1). The default exposure time of 8 hours is used for all postapplication assessment scenarios. The transfer coefficient for scouting was considered appropriate as a surrogate for intermediate-term duration for re-entry into treated industrial vegetation and non-cropland areas. The highest applicable transfer coefficient was used for short-term duration of re-entry into treated conifers.

3.4.2.2-1 Postapplication re-entry exposure and risk estimates for areas treated with Flazasulfuron 25WG Herbicide

Dislodgeable foliar residue (µg/cm^2)	Activity	Transfer Coefficient (cm^2/h)	Dermal Exposure [b] (mg/kg bw/day)	Short-term MOE [c] (target = 100)	Intermediate-term MOE [c] (target=100)
Industrial vegetation/non-cropland areas [a]					
0.125	Scouting	1100	0.0138	-------	145
Conifers, and conifer release (forestry) [d]					
0.125	Hand set irrigation (outdoor only)	1750	0.0219	2283	------

a. No TC available for re-entry into treated for industrial vegetation management. The TC for scouting of forage crops (ARTF) is considered representative of a worker scouting;

b. Dermal Exposure (mg/kg bw/day) = Dislodgeable foliar residue × Transfer coefficient × Exposure time × Dermal Absorption / Body Weight

Where,

Dislodgeable foliar residue = maximum application rate (0.50 µg/cm^2) × 25% dislodgeable residue on the day of application;

Transfer coefficient (cm^2/h), from ARTF database;

Exposure time, 8 hours/day;

Dermal absorption, 100%;

Body Weight (kg), adult (80 kg)

c. MOE = NOAEL / Exposure

Where,

NOAEL (oral) = 50 mg/kg bw for short-term duration exposures; 2 mg/kg bw for intermediate-term duration exposures; Target MOE = 100.

d. Highest applicable transfer coefficient for forestry conifer release and conifers (outdoor container- and field grown, ornamental and Christmas trees); addresses less intensive tasks such as scouting.

Risks are not of concern for workers entering treated conifers, conifer release (forestry), industrial vegetation, and non-cropland areas on the day of application. The standard -REI of 12 hours after a treatment will be maintained for worker re-entry to vineyards, conifers (field- and container-grown), and forestry conifer release sites. The REI for treated industrial vegetation and non-cropland areas (non-military and military sites) will be ‘Do not enter or allow others to enter treated areas until sprays have dried’.

3.4.3 Residential Exposure and Risk Assessment

No risk assessments are required, as Flazasulfuron 25WG is not intended to be used in residential areas.

3.4.4 Bystander Exposure and Risk

3.4.4.1 Application

Bystander exposure should be negligible since the potential for drift during application is expected to be minimal. Applications to grapes and conifers are in areas restricted to public access and the public is not expected to be in non-cropland areas during treatment.

Applications are conducted 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. Therefore, bystander exposure during applications is not of concern.

3.4.4.2 Postapplication

There is potential for short-term exposure to flazasulfuron for adults (16+), youth (11<16 years old) and children (6<11 years old) from entering treated non-cropland areas, such as hiking along roadsides, rights-of-way, and in forested areas that have recently been treated, and other non-crop areas indicated on the label.

No transfer coefficient is available for re-entry into treated industrial and non-cropland vegetation. The surrogate transfer coefficient used is scouting of orchard crops and forestry from the ARTF database, which is expected to be representative of a person hiking or walking within treated industrial vegetation or forested areas. The adult transfer coefficient of 580 cm^2/h was scaled from the adult (16<81 years old) mean body surface area of 1.95 m^2 to the surface area of youth (11<16 years old, 1.59 m^2) and child (6<11 years old, 1.08 m^2) (SPN2014-01), and normalized with the age-range-specific body weights. Bystander exposures to flazasulfuron are presented in Table 3.4.4.2-1.

Table 3.4.4.2-1 Postapplication risks for bystanders entering non-cropland or forested sites treated with Flazasulfuron 25WG Herbicide

Dislodgeable foliar residue [a] ($\mu g/cm^2$)	Activity	Sub-population	Transfer Coefficient (cm^2/h) [b]	Dermal Exposure [c] (mg/kg bw/day)	MOE [d] (target = 100)
0.125	Hiking	Adult (16+ yrs old)	580	0.0018	27778
		Youth (11<16 yrs old)	476	0.0021	23810
		Child (6<11 yrs old)	319	0.0025	20000

a. DFR value on the day of application; single treatment at 50 g a.i./ha × 10^6 µg/g × 10^{-8} ha/cm^2 × 25%;
b. No Transfer coefficient (cm^2/h) available for re-entry into industrial vegetation management; therefore, scouting orchard crops and forestry used as a surrogate (ARTF, database). Transfer coefficient of 580 cm^2/h was scaled from the mean adult body surface area to youth and child, respectively (SPN2014-01);
c. Dermal Exposure (mg/kg bw/day) = Dislodgeable foliar residue × Transfer coefficient × Exposure time × Dermal Absorption / Body Weight
Where,
Dislodgeable foliar residue, on the day of application (0.125 $\mu g/cm^2$);
Transfer coefficient (cm^2/h), see (b) above;
Exposure time (h) is 2 hours/day for all populations (USEPA, Exposure Factors Handbook, 2011)
Dermal absorption (%), 100%
Body Weight, adult body (80 kg); youth (57 kg); and child (32 kg)
d. Margin of Exposure (MOE) = NOAEL / Exposure
Where,
NOAEL (oral) = 50 mg/kg bw, short-term endpoint.

Health risks are not of concern for bystanders entering treated industrial vegetation and conifers on the day of application.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in grape commodities is flazasulfuron. The data gathering and enforcement analytical method is valid for the quantitation of flazasulfuron residues in grape matrices. The residues of flazasulfuron are stable in grapes for up to 12 months when stored in a freezer at <-20°C. The raw agricultural commodity grapes were processed into grape pomace, juice and raisins, but no processing factors could be determined due to the lack of quantifiable residues in both RAC and the processed commodities. Crop field trials conducted throughout the United States using an end-use product containing flazasulfuron at exaggerated rates in or on grapes are sufficient to support the proposed maximum residue limit.

3.5.2 Dietary Risk Assessment

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

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the basic chronic non-cancer analysis for flazasulfuron: 100% crop treated, default processing factors (where available), the proposed Canadian MRL and the American tolerances. The basic chronic dietary exposure from all supported flazasulfuron food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 1.1% of the acceptable daily intake (ADI). Aggregate exposure from food and drinking water is considered acceptable. The PMRA estimates that chronic dietary exposure to flazasulfuron from food and drinking water is 17.3% (0.001728 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for all infants (< 1 year) at 64% (0.006372 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

The following assumptions were applied in the basic acute analysis for flazasulfuron: 100% crop treated, default processing factors, the proposed Canadian MRL and the American tolerances. The basic acute dietary exposure (food alone) for all supported flazasulfuron registered commodities is estimated to be 0.03% (0.000131 mg/kg bw/day) of the ARfD for general population (95^{th} percentile, deterministic). Aggregate exposure from food and drinking water is considered acceptable: 1.0% of the ARfD for the general population.

3.5.3 Aggregate Exposure and Risk

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

3.5.4 Maximum Residue Limits

Table 3.5.4 Proposed Maximum Residue Limit

Commodity	Recommended MRL (ppm)
Grapes	0.01

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

The nature of the residues in plant matrices, analytical methodologies, field trial data, and acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 6 and 7.

3.6 Exposure From Drinking Water

3.6.1 Concentrations in Drinking Water

The PMRA estimates the concentration of pesticides in potential drinking water sources and incorporates these estimates into aggregate exposure assessments as part of the process of determining the potential impact of pesticide use on the health of Canadians. Estimated environmental concentrations (EECs) of flazasulfuron combined residues (flazasulfuron plus its five break down products: DTPU, DTPP, HTPP, TPSA, and ADMP) in potential drinking water sources (groundwater and surface water) were generated using computer simulation models. EECs of flazasulfuron combined residues in groundwater were calculated using the Pesticide in Water Calculator (PWC) model to simulate leaching through a layered soil profile over a 50-year period. The concentrations calculated using PWC are average concentrations in the top 1 m of the water table. EECs of flazasulfuron combined residues in surface water were estimated in a vulnerable drinking water source, a small reservoir, using the PWC model. It simulates pesticide runoff from a treated field into an adjacent water body and the fate of a pesticide within that water body. An overview of how the EECs are estimated is provided in the PMRA's Science Policy Notice SPN2004-01, *Estimating the Water Component of a Dietary Exposure Assessment.*

A Level 1 drinking water assessment was conducted for combined residues, using conservative assumptions with respect to environmental fate, application rate and timing, and geographic scenario. Due to lack of studies on the fate of breakdown products, the most conservative approach was used in estimating fate parameters (Table 3.6.1-1). Ten initial application dates between mid-March and mid-July were modelled. The model was run for 50 years for all scenarios. The highest EECs of all selected runs are reported in Table 3.6.1-2.

Table 3.6.1-1 Major groundwater and surface water model inputs.

Parameter	Value
Application Information	
Crop(s) to be treated	Grapes
Maximum rate each application (g a.i./ha)	50
Maximum number of applications per year	1
Method of application	Ground foliar
Environmental Fate Characteristics	
Hydrolysis half-life at pH 7 (days)	Stable
Photolysis half-life in water (days)	30
Adsorption K_{oc} (mL/g)	43 (20th percentile of six K_{oc} values for flazasulfuron)
Aerobic soil biotransformation half-life (days)	Stable
Aerobic aquatic biotransformation half-life (days)	147 (the longer of the half- lives of two labels)
Anaerobic aquatic biotransformation half-life (days)	15 (the longer of the half-lives of two labels)

Table 3.6.1-2 Level 1 estimated environmental concentrations of flazasulfuron combined residue in potential drinking water sources.

Crop/use pattern	Groundwater EEC (µg a.i./L)		Surface Water EEC (µg a.i./L)	
			Reservoir	
	Daily[1]	Yearly[2]	Daily[3]	Yearly[4]
Grapes (1 × 50 g a.i./ha)	84	84	4.3	0.56

Notes:
1 90th percentile of daily average concentrations
2 90th percentile of 365-day moving average concentrations
3 90th percentile of the peak concentrations from each year
4 90th percentile of yearly average concentrations

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Flazasulfuron is highly soluble in water over a pH range of 5-7 (27-2100 mg/L) and is unstable in alkaline waters. It has low potential to volatilize from moist soils or from water into the air due to its low vapour pressure ($<1.33 \times 10^{-5}$ Pa) and low Henry's Law Constant (2.55×10^{-11} Pa·m^3·mol^{-1}). Flazasulfuron is not expected to bioaccumulate in organisms due to its high water solubility and low octanol-water partitioning coefficient (log K_{ow} -0.06-1.30).

In the terrestrial environment, hydrolysis is expected to be the most significant route of dissipation of flazasulfuron with hydrolysis half-life of 0.80–17 days. Hydrolysis rate is faster in acidic soils (pH<6), forming four major transformation products, DTPU, DTPP, TPSA and ADMP. Phototransformation and biotic transformation are not important routes of dissipation for flazasulfuron in soils. Flazasulfuron may be classified as non-persistent to moderately persistent in aerobic soil with half-lives ranging from 12-124 days based on the results of the laboratory studies. Field studies, however, showed that it is non-persistent and half of the applied amount of flazasulfuron can dissipate within 4-7 days. The dissipation rates depended on the characteristics of the soils, in particular pH, with dissipation appearing faster in acidic soils. Transformation products of flazasulfuron are stable to hydrolysis but may transform further by phototransformation and/or biotransformation, which could contribute to the overall degradation of flazasulfuron in the environment. The field and laboratory results indicated that transformation products of flazasulfuron are more persistent than flazasulfuron, in particular, TPSA is very persistent.

Similar to soil, the pathway of dissipation of flazasulfuron appears to proceed initially with hydrolysis in the water/sediment system, and the products of hydrolysis can undergo further transformation in aerobic and anaerobic aquatic systems. HTPP is identified as a major biotransformation product in aquatic systems from demethylation of DTPP. Half- life of flazasulfuron is 24 days in aerobic water/sediment system under laboratory conditions, indicating that flazasulfuron is slightly persistent under aerobic aquatic systems. Given that hydrolysis is pH-dependent and is faster in acidic than in neutral or alakaline environment, flazasulfuron may be more persistent in a non-acidic environment.

Laboratory adsorption/desorption studies indicate that flazasulfuron and its major transformation products are mobile. Based on the adsorption/desorption characteristics, aged-column leaching studies, criteria of Cohen et al. (1984), the groundwater ubiquity score of Gustafson (1989), and the result of the water modelling, flazasulfuron and its transformation products have the potential to reach ground and surface waters at sites where conditions favor greater persistence and mobility. However, terrestrial field studies show limited vertical movement of these products. Flazasulfuron and its transformation products are not expected to carry over in significant amounts (≥ 30%) into the next growing season.

Flazasulfuron is unlikely to bioaccumulate in organisms. It is not expected to volatilize from water and moist soils, and long-range atmospheric transport is unlikely to occur.

The fate and behaviour of flazasulfuron in the environment is summarized in Appendix I, Table 8.

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 EECs with concentrations at which adverse effects occur. 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 conservative exposure scenarios (for example, 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 for most species, 0.4 for pollinators and 2 for beneficial arthropods). If the screening level risk quotient is below the LOC, 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 LOC, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

A risk assessment for flazasulfuron and its transformation products (based on available toxicity data for transformation products) was conducted for terrestrial organisms. For acute toxicity studies, uncertainty factors of 1/2 and 1/10 the EC_{50} (LC_{50}) are typically used in modifying the toxicity values for terrestrial invertebrates, birds and mammals when calculating risk quotients (RQs). No uncertainty factors are applied to chronic no observed effect concentration (NOEC) endpoints. Risk quotients for flazasulfuron and its transformation products were calculated based on the highest maximum seasonal application rate of 50 g a.i./ha. A summary of terrestrial toxicity data for flazasulfuron is presented in Appendix I, Table 9 and the accompanying risk assessment is presented in Appendix I, Table 10 for terrestrial organisms (other than bees, birds and wild mammals), Appendix I, Table 11 for bees and Appendix I, Table 12 for birds and wild mammals.

Multiple EC_{50} values were available for terrestrial vascular plants and the program ETX 2.1 was used to generate species sensitivity distributions (SSDs) based on normally distributed toxicity data. The hazardous concentration to 5% of the species (HC_5) was then calculated for vegetative vigour (the most sensitive endpoints) from their respective SSDs. The HC_5 is the concentration which is protective for 95% of species of a taxonomic group (in this case terrestrial vascular plants).

At the HC_5 exposure level, 5% of all terrestrial vascular plants will be exposed to a concentration which exceeds their LC_{50} toxicity value. The HC_5 values were used to calculate the risk quotients for terrestrial vascular plants instead of the most sensitive species tested. This provides a more scientifically robust endpoint, which uses all of the data (Appendix I, Table 13).

Earthworms: The risk quotient for earthworms resulting from acute exposure to flazasulfuron does not exceed the LOC at the screening level. The use of flazasulfuron is expected to pose a negligible risk to earthworms on an acute basis.

Bees: The risk quotients for adult bees and larvae resulting from acute and chronic exposure to flazasulfuron do not exceed the LOC at the screening level. The use of flazasulfuron is expected to pose a negligible risk to bees.

Beneficial arthropods: The risk quotients for predatory and parasitic arthropods resulting from exposure to flazasulfuron do not exceed the LOC at the screening level. Therefore, use of flazasulfuron is expected to pose a negligible risk to beneficial arthropods.

Birds: The risk quotients for birds resulting from acute oral and reproduction exposure to flazasulfuron did not exceed the LOC at the screening level. Therefore, use of flazasulfuron is not expected to pose risks to birds.

Wild Mammals: The risk quotients for wild mammals resulting from acute oral and reproduction exposure to flazasulfuron did not exceed the LOC at the screening level. Therefore, flazasulfuron is expected to pose negligible risk to wild mammals.

Terrestrial Vascular plants: The risk quotient values did not exceed the level of concern for seedling emergence. Using HC_5 value from the SSDs for vegetative vigour, the calculated risk quotient values for all intended uses exceed the LOC, indicating that the proposed uses of Flazasulfuron 25WG Herbicide adversely affect non-target terrestrial plants. It is expected that the transformation products have less than or similar effects to non-target terrestrial plants.

A refined risk assessment was undertaken to characterize the risk to non-target plants due to spray drift of 6% for ground application with medium droplet size. The risk quotient values for vegetative vigour of terrestrial plants from off-field exposure did exceed the level of concern, therefore, there is a potential risk to non-target terrestrial plants from off-field exposure at the proposed application rate of Flazasulfuron 25WG Herbicide (Appendix I, Table 14). Risk mitigation measures, such as spray buffer zones are required for Flazasulfuron 25WG Herbicide to protect terrestrial vascular plants.

4.2.2 Risks to Aquatic Organisms

A risk assessment for flazasulfuron and its transformation products (based on available toxicity data for transformation products) was conducted for freshwater and marine aquatic organisms. A summary of aquatic toxicity data is presented in Appendix I, Tables 15 and 16.

For acute toxicity studies, uncertainty factors of 1/2 the EC_{50} (LC_{50}) are typically used for aquatic plants, and invertebrates, and 1/10 for fish species when calculating RQs. No uncertainty factors are applied to chronic NOEC endpoints. A screening level risk assessment for aquatic organisms was conducted assuming a direct overspray to water. Two scenarios were considered for exposure to aquatic organisms. Scenario 1: EEC in 80 cm water depth, used for a permanent water body and Scenario 2: EEC in 15 cm water depth, used for a seasonal water body. If the screening level risk quotient is equal to or greater than the level of concern of one, then a refined risk assessment is performed to further characterize the risk.

Invertebrates: The risk quotients for freshwater and marine invertebrates resulting from exposure to flazasulfuron and its transformation products do not exceed the LOC, indicating that the proposed uses of Flazasulfuron 25WG are expected to pose negligible risk to freshwater and estuarine/marine invertebrates.

Fish and amphibians: The risk quotients for freshwater and marine fish resulting from exposure to flazasulfuron and its transformation products do not exceed the LOC at the screening level. The use of flazasulfuron is not expected to pose a risk to fish.

In the absence of toxicity studies on amphibians, the toxicity values from the most sensitive fish were used to calculate the RQ for amphibians. The risk quotients for amphibians do not exceed the LOC at the screening level, therefore, the use of flazasulfuron is not expected to pose a risk to amphibians.

Aquatic Plants: The screening level risk quotient for green algae and aquatic vascular plants resulting from exposure to flazasulfuron exceeds the LOC at the screening level. It is expected that the transformation products have less than or similar effects to non-target terrestrial plants. The risk to aquatic plants was further characterized by looking at exposure from spray drift and runoff. Based on the risk quotients using the off-field EEC from spray drift (6% of the application rate), the LOC for aquatic vascular plants was exceeded (Appendix I, Table 9). Spray buffer zones will be required on the label of the end-use product, Flazasulfuron 25WG Herbicide, to protect non-target aquatic vascular plants.

Based on the risk quotients using the EECs from runoff into 80 cm of waterbody (Appendix I, Table 17) for all regions of use, the LOC for aquatic vascular plants was exceeded (Appendix I, Table 18); however, the exceedance of the LOC is due in part to the highly conservative nature of the screening level of modelling, which includes the use of endpoints from laboratory studies and an assumption of immediate run-off after application. Consideration has also been given to terrestrial field dissipation studies that show that the dissipation of flazasulfuron under field conditions is significantly faster than the laboratory studies that were used for modelling (reaching 50% of the initial concentration in less than one week under field conditions versus a laboratory half-life in soil ranging from 12 days to several months). In addition, flazasulfuron is applied only once per year and in the presence of water it breaks down quickly. The effects of flazasulfuron on aquatic plants are of sublethal nature and a study showed that aquatic vascular plants were recovered completely after 7 days of exposure. This study also showed that there were no statistically significant differences between control and treated colonies. Furthermore, flazasulfuron has been used in the United States (for almost 20 years) and in Europe for many

years without any significant adverse effects reported on aquatic plants. Therefore, the potential impact on aquatic vascular plants based on the predicted screening level risk quotients is unlikely to occur in Canada under the proposed use pattern of a single application. Label statements to mitigate runoff into aquatic habitats are required on the label for the end-use product, Flazasulfuron 25WG Herbicide.

5.0 Value

5.1 Consideration of Benefits

Flazasulfuron 25WG Herbicide provides pre- and postemergent control of grasses, broadleaf weeds, and sedges, with residual activity and tank-mix flexibility. It controls a broad spectrum of weeds, including key weeds which are present in agricultural and forestry systems, such as ragweed, pigweed, nightshade, and lamb's quarters. Flazasulfuron was identified as a priority for the control of broadleaf weeds in Christmas trees by Canadian growers.

Flazasulfuron has been registered in the United States for the same uses since 2012. The registration of Flazasulfuron 25WG Herbicide provides Canadian growers with access to a product that is already available in the United States.

Flazasulfuron is a herbicide with a new mode of action for use in grapes and conifer trees. The registration of Flazasulfuron 25WG Herbicide provides a useful tool for managing weeds in these sites, especially for weeds that have developed resistance to other modes of action (Appendix I, Table 19). The additional mode of action provided by flazasulfuron can also aid resistance management through rotation of active ingredients in grapes and conifer trees.

The application of Flazasulfuron 25WG Herbicide is compatible with current management practices, including integrated pest management (IPM), and does not interfere with preventative measures for weeds, such as use of ground covers and mulches.

5.2 Effectiveness Against Pests

Efficacy information submitted for review included data from 127 field research trials which were conducted in the United States and Canada between 2002 and 2014. Fifty-three trials were conducted in grapes, 38 trials in Christmas trees, and 36 trials in non-crop areas. Efficacy of Flazasulfuron 25WG Herbicide applied pre- and postemergence alone at various rates or in tank-mix with various other herbicides was evaluated.

The trial data demonstrated control or suppression of the listed weeds that occur in Canada with either pre- or postemergent application of Flazasulfuron 25WG Herbicide at 150-200 g/ha (Appendix I, Table 20). The higher application rate is for larger weeds and heavier infestations. For postemergent application, a NIS at 0.25% v/v or COC or MSO at 1.0% v/v is required.

For improved burndown weed control, Flazasulfuron 25WG Herbicide may be applied with Ignite SN or Ignite 15SN or glyphosate herbicides, which are labelled for the same use pattern.

For longer residual weed control, Flazasulfuron 25WG Herbicide may be applied with Karmex XP, Karmex DF, Diurex 80W, Alligare Diuron 80W, Simadex Simazine Flowable, Princep Nine-T, or Simazine 480.

5.3 Phytotoxicity to Host Plants

Grapes: Crop tolerance of 11 grape varieties following the application of Flazasulfuron 25WG Herbicide at the labelled rate and exaggerated rates, or in tank-mix with various herbicides was evaluated in 30 trials, which were conducted in California, Michigan, Washington, and New York between 2002 and 2012.

The trial data demonstrated that Flazasulfuron 25WG may be applied as a directed spray to grape vines established for at least three years. Use of a protective sleeve is required for the 3rd year vines to minimize injury potential.

Conifer Trees: Crop tolerance of balsam fir, Fraser fir, grand fir, nordman fir, white fir, blue spruce, Norway spruce, eastern white pine, red pine, Scotch pine, Virginia pine, white pine, Douglas fir, and Leyland cypress following over-the-top application of the same herbicide treatments was evaluated in 33 trials.

The trial data demonstrated that Flazasulfuron 25WG may be applied over-the-top to conifers, which are established for more than a year, prior to spring bud break or when conifers are sufficiently hardened off. Directed applications are recommended to reduce injury potential, particularly for conifers that have new growth or are not sufficiently hardened off.

Rotational crop tolerance is not of concern since grapes and conifers are usually not grown in rotation.

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 review process, flazasulfuron and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Flazasulfuron does not meet all Track 1 criteria, and is not considered a Track 1 substance. See Appendix I, Table 21 for comparison with Track 1 criteria.

- There is not enough information to assess the flazasulfuron transformation products against the TSMP criteria; however, the transformation products are not expected to meet all the Track 1 criteria, considering chemical structure, high solubility and knowledge of flazasulfuron K_{ow}. They are not expected to form in significant quantities in the environment.

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 conclusions:

- Technical grade flazasulfuron and the end-use product Flazasulfuron 25WG 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.

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

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, *Formulants Policy and Implementation Guidance Document.*

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for flazasulfuron is adequate to define the majority of toxic effects that may result from exposure. In short- and long-term studies in laboratory animals, toxicity of flazasulfuron was manifested mainly by the effects on the liver and kidneys. There was no evidence of oncogenic potential of flazasulfuron in rats or mice. There was no evidence of increased susceptibility of the young in reproductive or developmental toxicity studies. In the rabbit developmental toxicity study, abortions were preceded by cessation of food intake and reduction of body weights. Flazasulfuron was not neurotoxic after single and repeat-dose administration. Flazasulfuron was not immunotoxic in mice. 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.

Mixers, loaders, and applicators handling Flazasulfuron 25WG Herbicide, and workers re-entering treated vineyards, industrial vegetation and conifers, are not expected to be exposed to levels of flazasulfuron that will result in unacceptable risks when used according to label directions. The personal protective equipment on the product label and other precautionary statements are adequate to protect workers.

Bystander exposures are not expected to result in unacceptable risks when Flazasulfuron 25WG Herbicide is used according to label directions.

The nature of the residues in grapes is adequately understood. The residue definition for enforcement and risk assessment is flazasulfuron for grapes. The proposed use of flazasulfuron on grapes does not constitute a risk of concern for acute or chronic dietary exposure (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 the MRL. The PMRA recommends that the following MRL be specified for residues of flazasulfuron.

Commodity	Recommended MRL (ppm)
Grapes	0.01

7.2 Environmental Risk

The use of Flazasulfuron 25WG Herbicide, containing the active ingredient flazasulfuron, may pose a risk to non-target terrestrial and aquatic vascular plants. As a result, spray buffer zones to protect sensitive terrestrial and aquatic habitats from spray drift, and label statements to inform users of the potential risks to plants are required. In addition, specific instructions are provided to prevent runoff into aquatic habitats.

7.3 Value

Flazasulfuron was identified as a priority for control of broadleaf weeds in Christmas trees by Canadian growers. The registration of Flazasulfuron 25WG Herbicide provides Canadian growers not only with access to a product that is currently available in the United States for the same uses, but also a new mode of action for managing weeds in grapes and conifer trees. Flazasulfuron 25WG Herbicide may be particularly useful in managing weeds that have developed resistance to other modes of action.

Value information demonstrated that the pre- and postemergent applications of Flazasulfuron 25WG Herbicide provided acceptable control of the listed weeds, that grapes and conifer trees exhibit an adequate margin of crop tolerance to Flazasulfuron 25WG Herbicide applied in accordance with the label instructions, and that Flazasulfuron 25WG Herbicide is compatible with listed tank-mix partners.

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 Technical Flazasulfuron Herbicide and Flazasulfuron 25WG Herbicide, containing the technical grade active ingredient flazasulfuron, for pre- and postemergent control or suppression of grasses, broadleaf weeds and sedges in grapes, conifer trees and industrial vegetation management sites.

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

>	Greater than
≥	Equal or greater than
<	Less or lower than
↓	decrease
%	percentage
♂	Male organism symbol
♀	Female organisms symbol
µg	micrograms
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
ADMP	4,6-dimethoxypyrimidin-2-amine
AFC	splenic antibody-forming cell assay
AHETF	Agricultural Handlers Exposure Task Force
ALS	acetolactate synthase
AR	Applied radioactive
ARfD	acute reference dose
ARTF	Agricultural Reentry Task Force
ASAE	American Society of Agricultural Engineers
ATPD	Area-treated-per-day
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
bw	body weight
bwg	body-weight gain
^{14}C	Carbon-14 radioactive isotope
°C	degree (s) Celsius
C_{max}	time to maximum concentration
CAF	composite assessment factor
CAS	Chemical Abstracts Service
CEPA	Canadian Environmental Protection Act
cm	centimetres
CO_2	Carbon dioxide
COC	crop oil concentrate
d	day
DF	dry flowable
DFR	dislodgeable foliar residue
DMPU	l-(4,6-dimethoxypyrimidin-2-yl)urea
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
dw	dry weight
DTPU	N-(4,6-Dimethoxy-2-pyrimidinyl)-N-[3-(trifluoromethyl)-2-pyridinyl]urea
DTPP	4,6-Dimethoxy-N-[3-(trifluoromethyl)-2-pyridinyl]-2- Pyrimidinamine
EC_{25}	effective concentration on 25% of the population
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure

EEC	estimated environmental concentration
EL	Early life stage
EPA	U. S. Environmental Protection Agency
EU	European Commission
g	gram
2, 3-GTF	3-trifluoromethyl-2-pyridylguanidine
h	hour(s)
ha	hectare(s)
HAFT	highest average field trial
HDT	highest dose tested
HPLC	high performance liquid chromatography
HTPP	4-hydroxy-6-methoxy-2-(3-trifluoro-methyl-2-pyridylamino)pyrimidine
HTF	2-hydroxy-3- triluoromethylpyridine
IPM	integrated pest management
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
M	molar
mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
MSO	methylated seed oil
N/A	not applicable
NAFTA	North American Free Trade Agreement
NIS	non-ionic surfactant
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
OC	organic carbon content
OM	organic matter content
(P)	radiolabel at the pyridine ring
PBI	plantback interval

PCPA	*Pest Control Product Act*
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
pK_a	dissociation constant
(Pm)	radiolabel at the pyrimidine ring
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PWC	Pesticide in Water Calculator
RAC	raw agricultural commodity
RD	residue definition
RQ	risk quotient
SC	soluble concentrate
SL-160	code name for flazasulfuron
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TGAI	technical grade active ingredient
TP	transformation products
TPSA	3-Trifluoromethyl-2-pyridinesulfonamide
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution
WG	wettable granule
w/w	weight per weight ratio
WHC	water holding capacity
wt(s)	weight(s)

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Soil / Sediment	CCRL-MTH-045	Flazasulfuron DTPU TPSA DTPP ADMP	HPLC-MS/MS	2.5 ng/g	soil	2551367
Water	GPL-MTH-082	Flazasulfuron DTPU DTPP	HPLC-MS/MS	0.05 µg/L	surface water/ drinking water	2552370 2551371
		TPSA		0.20 µg/L		
Plants	S09-03106 (enforcement)	Flazasulfuron	LC-MS/MS	0.01 ppm	Olive, wheat and tomato	2581941 2551258
Animal	6954-96-0200-MD-001	Flazasulfuron	HPLC-UVD	10 ng/g	beef muscle/ cow's milk/ chicken muscle/ beef liver	2551372

Table 2 Identification of Metabolites

SL-160	flazasulfuron
HDTG + TPPG	4,6-dimethoxy-2-[[3-(trifluoromethyl)-2-pyridyl]amino]-5-pyrimidinyl glucopyranosiduronic acid
	1-β-[2-(3-trifluoromethyl-2-pyridylamino)-6-methoxy-4-pyrimidyloxy]glucopyranuronic acid
DTPU	1-(4,6-dimethoxypyrimidin-2-yl)-1-[3-(trifluoromethyl)pyridin-2-yl]urea
HDPU	l-(5-hydroxy-4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulphonyl)urea
HTPP	4-hydroxy-6-methoxy-2-(3-trifluoro-methyl-2-pyridylamino)pyrimidine
MTMG	3-(trifluoromethyl)-2-pyridyl 1-thio-glucopyranosiduronic acid
TPSA	3-(trifluoromethyl)-2-pyridinesulfonamide
ADMP	4,6-dimethoxypyrimidin-2-amine
HDU	1-(5-hydroxy-4,6-dimethoxypyrimidin-2-yl)urea

Table 3 Toxicity Profile of Technical Flazasulfuron Herbicide (SL-160)

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons. Organ weight effects reflect both absolute organ weights and relative organ to bodyweights unless otherwise noted. Effects seen above the LOAEL(s) have not been reported in this table for most studies for reasons of brevity.)

Study Type /Animal/PMRA #	Study Results
Metabolism/Toxicokinetic, oral (gavage, single dose and repeat dosing) Rat, Sprague-Dawley ^{14}C-SL-160 (P) and ^{14}C-SL-160 (Pm) (2 and 50	**Absorption:** After oral administration of ^{14}C-SL-160 (P) or ^{14}C-SL-160 (Pm), flazasulfuron was rapidly and well absorbed with peak plasma concentrations (C_{max}) reached in both sexes within 0.5 hours and 4-6 hours at the low and high dose, respectively. The bile cannulation studies confirmed the rapid absorption. By 48 h post exposure, males and females absorbed 93-99% of the low dose and 84-93% of the high dose. At 168 h, the blood concentration decreased to <1.7% of C_{max}. **Tissue distribution:** Radioactivity in tissues after single or repeat oral dose administration was

Study Type /Animal/PMRA #	Study Results
mg/kg bw, single dose) ^{14}C-SL-160 (P) and ^{14}C-SL-160 (Pm) (2 mg/kg bw/d, repeated dosing for 15 days)(for distribution and excretion) PMRA# 2551355, 2551356, 2551357, 2551358, 2551359, 2551360, 2551361, 2551362, 2551363	low, ≤3.9%AD in males and <1%AD in females. The absorbed radiolabel was mainly distributed in the blood, liver, muscle, carcass, and bone. **Metabolism:** Metabolism of SL-160 included molecular rearrangement, cleavage at the sulfonylurea bridges, oxidation, displacement, and glucuronic acid conjugation. Unchanged flazasulfuron accounted for the majority of radioactivity in urine, with lesser amounts in feces and bile. The major metabolites in the urine and feces were identified as HDTG+TPPG. Minor urinary and fecal metabolites were HDPU, HTPP, and DTPU. TPSA and MTMG were minor urinary metabolites and HDU and ADMP were identified in the feces. **Excretion:** Elimination of orally-administered flazasulfuron was rapid and extensive. Almost all administered dose (AD) was recovered in the excreta within 72 hours. Urine was the major route of excretion. Radioactivity in tissues after single or repeat oral dose administration was low, <4% AD in males and <1%AD in females. Urinary excretion in females was greater than in males, whereas fecal elimination in males was greater than in females. This sex difference in the route of elimination was independent of dose levels. The distribution and excretion of radiolabel following pretreatment of multiple non-radiolabeled doses was not significantly different from that following administration of a single radiolabeled dose. There were no substantial differences in pharmacokinetics of SL-160 that was labelled at the pyridine ring (^{14}C-SL-160 (P)) or the pyrimidine ring (^{14}C-SL-160 (Pm)).
Acute studies – flazasulfuron TGAI (SL-160)	
Study Type/ Animal/ PMRA#	Study Results
Acute oral Rat, SD (Crj:CD) PMRA# 2551311	LD_{50} >5000 mg/kg bw Low toxicity
Acute dermal Rat, SD (Crj:CD) PMRA# 2551313	LD_{50} >2000 mg/kg bw Low toxicity
Acute inhalation Rat, Fischer (F344/DuCrj) PMRA# 2551315	LC_{50} >5.99 mg/L Clinical signs: wetness around the nose, mouth, thoracic fur, and the anus, chromodacryorrhea and reddish brown stains around the nose and mouth day 1 of post-exposure Low toxicity
Eye irritation Rabbit, New Zealand White PMRA# 2551317	MAS = 1.57/110 Minimally irritating
Skin irritation Rabbit, New Zealand White PMRA# 2551319	MAS = 0/8 Non-irritating
Skin sensitization (Buehler) Guinea pigs PMRA# 2551321	Not a skin sensitizer
Short-term studies – flazasulfuron TGAI (SL-160)	
Study Type/ Animal/ PMRA#	Study Results
90-Day dietary Rat, Fischer PMRA# 2551323	NOAEL = 5000 ppm (♂ = 287, ♀ = 309 mg/kg bw/d) LOAEL = 1000 ppm (♂ = 57.1, ♀ = 61.5 mg/kg bw/d) Effects at LOAEL: ↓ bw & bwg, ↑ wts of liver and kidneys; kidney focal tubular atrophy & dilatation of proximal tubules (♂); ↓ food intake & food efficiency (♀),

Study Type /Animal/PMRA #	Study Results
90-Day oral (capsule) Dog, Beagle PMRA# 2551325	NOAEL ♂ = 2, ♀ = 10 mg/kg bw/d LOAEL ♂ = 10, ♀ = 50 mg/kg bw/d Effects at LOAEL: liver pathology (increased brown pigment, inflammatory cell infiltration)
1-Year oral (capsule) Dog, Beagle PMRA# 2551327	NOAEL = 2 mg/kg bw/d LOAEL = 10 mg/kg bw/d Effects at LOAEL: inflammatory cell infiltration in the liver
21-Day dermal Rabbit, New Zealand white PMRA# 2551329	NOAEL = 1000 mg/kg bw/d (HDT)
Long-term studies – flazasulfuron TGAI (SL-160)	
Study Type/ Animal/ PMRA#	Study Results
80-week dietary oncogenicity Mouse, CD-1 PMRA# 2551331	NOAEL: ♂ = 500 ppm (987 mg/kg bw/d), 3500 ppm (596 mg/kg bw/d) LOAEL: ♂ not established, ♀ = 7000 ppm (1166 mg/kg bw/d) Effects at LOAEL: ↓ bw, food intake (♀) No evidence of carcinogenicity
2-Year dietary / oncogenicity Rat, Fischer PMRA# 2551333	NOAEL ♂ = 40 ppm (1.3 mg/kg bw/d) ♀ = 400 ppm (16.5 mg/kg bw/d) LOAEL ♂ = 400 ppm (13.3 mg/kg bw/d) ♀ = 4000 ppm (172.6 mg/kg bw/d) Effects at LOAEL: ↓ bw, kidney pathology No evidence of carcinogenicity
Reproductive developmental toxicity studies – flazasulfuron TGAI (SL-160)	
Study Type/ Animal/ PMRA#	Study Results
2-Generation dietary reproductive Rat, CD PMRA# 2551336	Parental systemic toxicity: NOAEL: ♂ = 200 ppm (13.7 mg/kg bw/d), ♀ = 2000 ppm (155 mg/kg bw/d) LOAEL: ♂ = 2000 ppm (155 mg/kg bw/d), ♀ = 10000 ppm (760 mg/kg bw/d) Effects at LOAEL: ↓ bw, food; kidney pathology - enlargement, discolouration, dilated renal pelvis, granularity, nephropathy, and tubular dilatation (♂) Reproductive toxicity: NOAEL = 2000 ppm (♂ = 135, ♀ = 155 mg/kg bw/d) LOAEL = 10000 ppm (♀ = 760 mg/kg bw/d) based on ↓ birth wt at 2nd generation Offspring toxicity: NOAEL = 2000 ppm (♀ = 155.0 mg/kg bw/d) LOAEL = 10000 ppm (♀ = 760.2 mg/kg bw/d) Effects at LOAEL: ↓ pup wts in both generations
Developmental, oral gavage Rat, CD PMRA# 2551343	Maternal toxicity: NOAEL = 300 mg/kg bw/d LOAEL = 1000 mg/kg bw/d Effects at LOAEL: ↓ bw, food intake Developmental toxicity: NOAEL = 300 mg/kg bw/d LOAEL = 1000 mg/kg bw/d Effects at LOAEL: ↓ fetal bw, delayed skeletal ossification No evidence of sensitivity of the young.
Developmental, oral gavage Rabbit, New Zealand White PMRA# 2551345	Maternal toxicity: NOAEL = 150 mg/kg bw/d LOAEL = 450 mg/kg bw/d Effects at LOAEL: abortions Developmental toxicity: NOAEL = 150 mg/kg bw/d LOAEL = 450 mg/kg bw/d

Study Type /Animal/PMRA #	Study Results
	Effects at LOAEL: abortions No evidence of sensitivity of the young.
Genotoxicity toxicity studies – flazasulfuron TGAI (SL-160)	
Study Type/ Animal/ PMRA#	Study Results
Bacterial Rec-assay and reverse mutation assay (Ames test) PMRA# 2551347	Cytotoxic at high concentrations in Ames test Negative
In vitro mammalian cell gene mutation (mouse lymphoma L5178Y cells) PMRA# 2551349	Cytotoxicity: minimal Precipitation: ≥500 µg/mL Negative
In vitro chromosome aberration in Chinese hamster lung cells PMRA# 2551351	Cytotoxicity: $<1.0 \times 10^{-4}$ M Negative
In vivo mouse micronucleus assay ICR mice (bone marrow) PMRA# 2551353	No mortality or clinical signs Negative
Special toxicity studies – flazasulfuron TGAI (SL-160)	
Study Type/ Animal/ PMRA#	Study Results
2-Week oral Rat, Fischer PMRA 2694935	Mechanistic study examining correlation of kidney pathology and hyaline droplets (positive for α2u-globulin) in renal proximal tubular cells Inconclusive
Acute neurotoxicity, oral gavage Rat, Sprague-Dawley PMRA 2551340	Systemic toxicity: NOAEL = 50 mg/kg bw LOAEL = 1000 mg/kg bw Effects at LOAEL: ↓ motor activity at 5h post-dosing No evidence of selective neurotoxicity
90-Day dietary neurotoxicity Rat, Crl:CD(SD) PMRA# 2551342	Systemic toxicity: NOAEL = 300 ppm (♂ = 190, ♀ = 229 mg/kg bw/d) LOAEL = 10000 ppm (♂ = 649, ♀ = 732 mg/kg bw/d) Effects at LOAEL: ↓ bw, food intake No evidence of selective neurotoxicity
4-Week dietary immunotoxicity Mouse, CD-1 mice ♀ PMRA# 2551335	NOAEL = 6000 ppm: HDT No effects on spleen cellularity, or in specific activity and total spleen activity, as measured by the AFC assay

Table 4 Toxicity Profile of Flazasulfuron 25WG Herbicide (SL-160 25% WG)

(Effects are known or assumed to occur in both sexes unless otherwise noted; in such cases, sex-specific effects are separated by semi-colons)

Study	Study findings
Acute, oral Rat, SD PMRA# 2551237	LD_{50} : ♂ = 4694 (4188-5261); ♀ 4908 (4226-5700) mg/kg bw Low toxicity
Acute, dermal Rat, SD PMRA# 2551239	LD_{50} >2000 mg/kg bw Clinical signs: very slight erythema d 2-6 Low toxicity
Acute, inhalation Rat, Fischer PMRA# 2551241	LC_{50} >6.17 mg/L Low toxicity
Eye irritation Rabbit, New Zealand White PMRA# 2551243	MAS = 0.89/110 Minimally irritating
Skin irritation Rabbit, New Zealand White PMRA# 2551245	MAS = 0/8 Non-irritating
Skin sensitization (Buehler) Guinea pig PMRA# 2551247	Not a skin sensitizer

Table 5 Toxicology References Values

Exposure scenario	study	Point of departure and endpoint	CAF[1] / Target MOE[2]
Acute dietary	rat acute neurotoxicity	NOAEL = 50 mg/kg bw LOAEL = 1000 mg/kg bw, effect - transient ↓ motor activity	100
	ARfD = 0.5 mg/kg bw		
Repeated dietary	2-year rat oncogenicity	NOAEL = 1.3 mg/kg bw/d LOAEL = 13.3 mg/kg bw/d, effect - nephropathy	100
	ADI = 0.01 mg/kg bw/d		
Dermal and inhalation[3] short-term	rat acute neurotoxicity	NOAEL = 50 mg/kg bw LOAEL = 1000 mg/kg bw, effect - transient ↓ motor activity	100
Dermal and inhalation[3] intermediate-term	90-d dog oral	NOAEL = 2 mg/kg bw LOAEL = 10 mg/kg bw, effect - liver pathology (inflammatory cell infiltration, brown pigment)	100
Cancer	Cancer risk not required based on lack of oncogenic effects in the rat and mouse carcinogenicity studies and lack of a mutagenicity concern.		

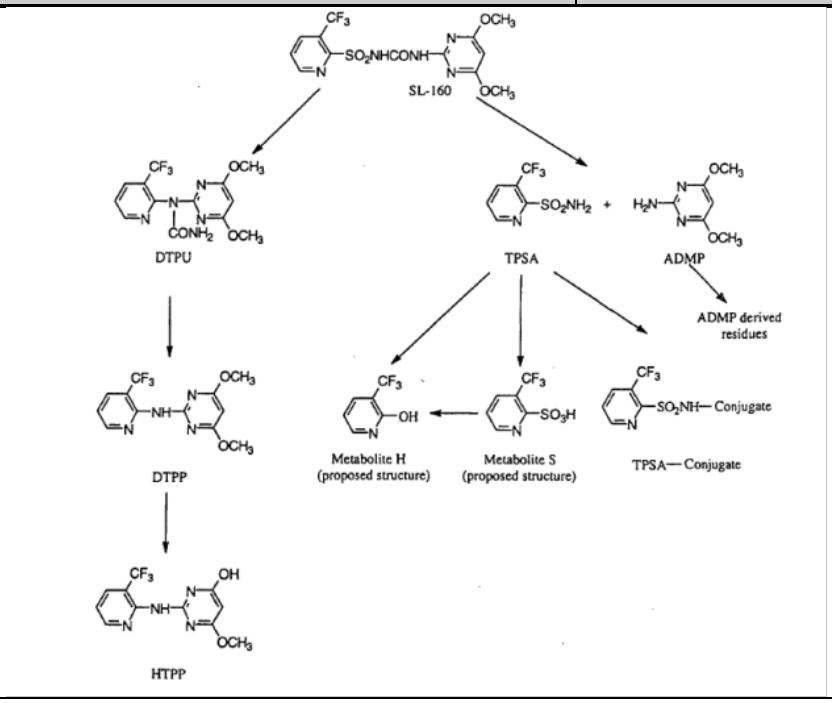
[1] CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessments
[2] MOE refers to a target MOE for occupational and residential assessments.

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

Table 6 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN GRAPE			**PMRA # 2551254**	
Radiolabel Position	[^{14}C-pyridyl]-flazasulfuron and [^{14}C-pyrimidinyl]-flazasulfuron			
Test Site	In individual pots in greenhouse and field outside			
Treatment	Soil treatment			
Total Rate	2 × 50 g a.i./ha; total rate of 100 g a.i./ha			
Formulation	Diluted in water			
Preharvest interval	85 days (field trial) and 34 days (greenhouse)			
Matrices	**PHI (days)**	**[^{14}C-pyridyl] TRRs (ppm)**		**[^{14}C-pyrimidinyl] TRRs (ppm)**
Grape fruit (field trial)	85	No sample		2.6
Grape leaves (field trial)	85	164.2		51.5
Grape fruit (greenhouse)	34	0.7		2.1
Grape leaves (greenhouse)	34	18.9		47.1
Metabolites Identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[^{14}C-pyridyl]**	**[^{14}C-pyrimidinyl]**	**[^{14}C-pyridyl]**	**[^{14}C-pyrimidinyl]**
Grape (field trial)	No sample	DTPU	No sample	Flazasulfuron, HTPP, DTPP
Grape (greenhouse)	DTPU	DTPU	Flazasulfuron, TPSA, HTPP, DTPP	Flazasulfuron, HTPP, DTPP
Grape leaves (field trial)	None	DTPU, DTPP	Flazasulfuron, DTPU, TPSA, HTPP, DTPP	Flazasulfuron, HTPP
Grape leaves (greenhouse)	DTPU	DTPU	Flazasulfuron, TPSA, HTPP, DTPP	Flazasulfuron, HTPP, DTPP
Proposed Metabolic Scheme in Plants				

NATURE OF THE RESIDUE IN GRAPE	PMRA # 2551254

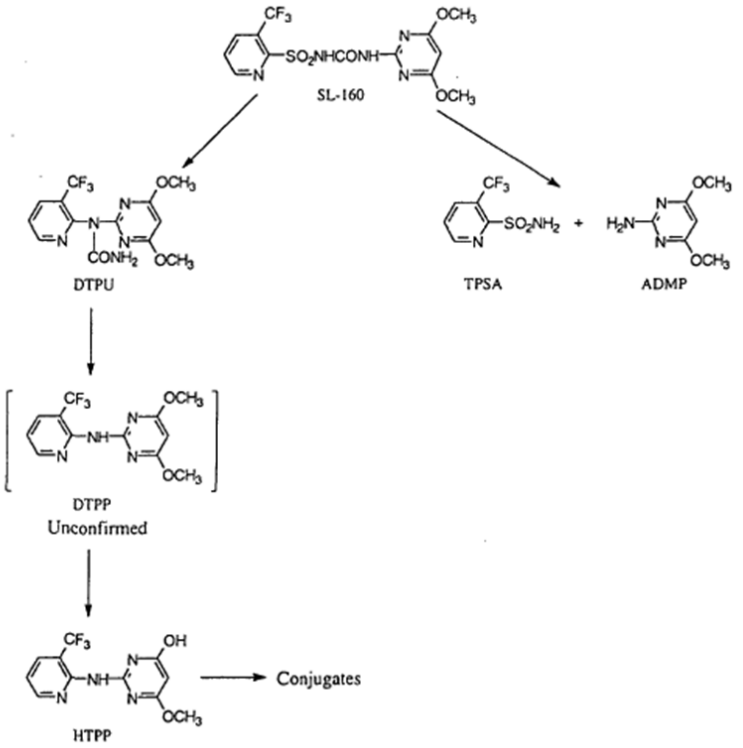


NATURE OF THE RESIDUE IN TOMATO	PMRA #s 2551255 and 2551256
Radiolabel Position	**[^{14}C-pyridyl]-flazasulfuron and [^{14}C-pyrimidinyl]-flazasulfuron**
Test Site	**In the field outside**
Treatment	**Foliar treatment**
Total Rate	**Once at 50 g a.i./ha**
Formulation	**Suspension concentrate (SC) formulation**
Preharvest interval	**83 days**

Matrices	**PHI (days)**	**[^{14}C-pyridyl]**	**[^{14}C-pyrimidinyl]**
		TRRs (ppm)	**TRRs (ppm)**
Tomato Juice	83	1.19	1.03
Tomato Pomace	83	0.365	0.321
Whole Tomato	83	1.55	1.35

Metabolites Identified	**Major Metabolites (>10% of the TRRs)**		**Minor Metabolites (<10% of the TRRs)**	
Radiolabel Position	**[^{14}C-pyridyl]**	**[^{14}C-pyrimidinyl]**	**[^{14}C-pyridyl]**	**[^{14}C-pyrimidinyl]**
Whole tomato	TPSA, HTPP conjugate	HTPP conjugate	DTPU, HTPP	DTPU, HTPP, ADMP
Proposed Metabolic Scheme in Plants				

NATURE OF THE RESIDUE IN TOMATO	PMRA #s 2551255 and 2551256



FREEZER STORAGE STABILITY	PMRA # 2551261

Plant matrices: Grapes

The freezer storage stability data indicate that residues of flazasulfuron are stable at -20°C for 12 months.

CROP FIELD TRIALS & RESIDUE DECLINE ON GRAPE	PMRA # 2551257

Field trials were conducted in 1996 in the United States. Trials were conducted in NAFTA Growing Regions 1 (2 trial), 10 (7 trials) and 11 (2 trials) for a total of 11 independent trials. Flazasulfuron 25WG was applied twice as soil applications at a rate of 72-102 g a.i./ha/application for a seasonal application rate of 167-177 g a.i./ha. An adjuvant at 0.25% (v/v) was included in the spray mixture at all test locations. The applications were made at 14-118 day re-treatment intervals with the last application occurring approximately 74-77 days before harvest.

Residue decline data show that residues of flazasulfuron were all <LOQ (0.01 ppm) with preharvest intervals (PHIs) of 55, 65, 75 and 85 days.

Commodity	Total Application Rate (g a.i./ha)	PHI (days)	Flazasulfuron Residue Levels (ppm)					
			n	LAFT	HAFT	Median	Mean	SD
Grapes	167-177	74-77	11	<0.01	<0.01	<0.01	<0.01	-

LAFT = Lowest Average Field Trial, HAFT = Highest Average Field Trial, SD = Standard Deviation.
Values based on per-trial averages. For computation, values < LOQ are assumed to be at the LOQ.
n = number of independent field trials.

PROCESSED FOOD AND FEED - Grape	PMRA # 2551257

Test Site	One trial in NAFTA Growing Region 10.
Treatment	Soil applications
Rate	Two applications with a total rate 1736 g ai/ha/season

NATURE OF THE RESIDUE IN TOMATO	PMRA #s 2551255 and 2551256
End-use product/formulation	Water-dispersible granular (WG) formulation of flazasulfuron
Preharvest interval	65 days
Processed Commodity	**Average Processing Factor**
Raisin	Flazasulfuron residues were all <LOQ (<0.01 ppm) in all grape processing commodities. Processing factors could not be calculated for flazasulfuron in grape processed fractions.
Grape juice	
Grape pomace	

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

PLANT STUDIES			
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crop: grape and tomato** **Rotational crops: none**		Flazasulfuron	
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crop: Grape** **Rotational crops: none**		Flazasulfuron	
Rationale for Residue Definition (RD)	While the major metabolite DTPU (in grapes) exceeds 10% of the TRRs, in absolute values they are significantly less than 0.01 ppm. Therefore, considering that the exposure to these metabolites will be low, there is no justification to include them in the risk assessment. Also, since flazasulfuron and DTPU are both <0.01 ppm, there is no need to include DTPU in the MRL since this would only add to the enforcement burden. This is also consistent with EPA and EU positions. Therefore, the residue definition for flazasulfuron in grapes for both enforcement and risk assessment purposes was determined to be flazasulfuron only.		
METABOLIC PROFILE IN DIVERSE CROPS		Not applicable	
DIETARY RISK FROM FOOD AND WATER			
Basic chronic non-cancer dietary exposure analysis **ADI = 0.01 mg/kg bw/day** **Estimated chronic drinking water concentration = 84 µg/L (Level I groundwater)**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Alone	**Food and Water**
	All infants < 1 year	0.3	63.7
	Children 1–2 years	1.1	24.5
	Children 3 to 5 years	0.9	19.9
	Children 6–12 years	0.5	14.6
	Youth 13–19 years	0.3	12.2
	Adults 20–49 years	0.2	17.1
	Adults 50+ years	0.2	16.6
	Females 13-49 years	0.2	16.8
	Total population	0.3	17.3
Basic acute dietary exposure analysis, 95th percentile	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Alone	**Food and Water**

ARfD = 0.5 mg/kg bw **Estimated acute drinking water concentration = 84 µg/L (Level I groundwater)**	**All infants < 1 year**	0.03	3.08
	Children 1–2 years	0.09	1.32
	Children 3 to 5 years	0.07	1.05
	Children 6–12 years	0.04	0.81
	Youth 13–19 years	0.02	0.76
	Adults 20–49 years	0.02	0.89
	Adults 50+ years	0.02	0.77
	Females 13-49 years	0.02	0.89
	Total population	0.03	0.90

Table 8 Fate and Behaviour of Flazasulfuron in the Environment

Property	Test substance	Value	Major Transformation Products	Comments	PMRA# and EPA MRID
Abiotic transformation					
Hydrolysis (22°C)	P-2 and Pm-5-labeled flazasulfuron	Half-life pH 4= 0.80 d pH 5= 3.84 d pH 7= 16.58 d pH 9= 12.84 d	**pH 4**: DTPU, TPSA, ADMP **pH 5**: DTPU, TPSA, ADMP **pH 7**: DTPU, DTPP **pH 9**: DTPP	Major route of dissipation	2551374 EPA: 46220949
Phototransformation on soil (pH 5.9, OC 0.9%, 25°C, WHC 75%)	P-2 and Pm-5-labeled flazasulfuron	Half-life 24 – 31 d based on a solar day (*10.2 hrs of artificial light, Xenon arc lamp, 449 W/m^2, was reported to be similar to that of natural sunlight at PTRL West, 37.45 EN latitude*). One soil, sandy loam.	DTPU, HTF, DMPU	Not a major route of dissipation-photoreaction is not associated with parent flazasulfuron, but with hydrolytic products. DTPP, TPSA and ADMP are minor transformation products. Light-exposed TPSA degrades to HTF and ADMP degrades to DMPU. HTF and DMPU are the photolysis products.	2551378 EPA: 46653501
Phototransformation in water (pH 7 at 22°C)	P-2 and Pm-5-labeled flazasulfuron	Half-life 18 d 12-hour light/12-hour dark cycle) *using a UV-filtered xenon arc lamp. The intensity and wavelength distribution of the artificial light were similar to natural sunlight in Painesville, Ohio on June 5, 1991.*	DTPU, Unidentified photoproduct	Not a major route of dissipation-photoreaction is not associated with parent flazasulfuron, but with hydrolytic products. DTPP and TPSA are minor transformation products. Insufficient information was provided on unidentified photoproduct.	2551380 EPA: 46220950
Phototransformation in air	Data are not provided/nor required.			Based on vapour pressure (<1.33 x10^{-5} Pa) and Henry's law	

Property	Test substance	Value	Major Transformation Products	Comments	PMRA# and EPA MRID
				constant (2.55×10^{-11} $Pa \cdot m^3 \cdot mol^{-1}$), volatilization of flazasulfuron from soil or water in the air is not expected.	
Biotransformation					
Biotransformation in aerobic soil (25°C and 20°C, WHC 75% and 50%)	P-2 and Pm-5-labeled flazasulfuron	Two US sandy loam soils, pH 5.8 & 5.5; three EU soils (pH 5.6, 6.4 & 7.6) Half-life 12 -124 d, using kinetics tool PestDF	DTPU, DTPP, TPSA, ADMP	All four transformation products are known to be products of hydrolysis. It is speculated that degradation initiated with hydrolysis, followed by biotransformation of hydrolytic products. Transformation product, HTPP (max 7% of AR) is considered a product of aerobic biotransformation formed by demethylation of DTPP.	2551382/ 2551383 EPA: 46220951/ 46220952
Biotransformation in anaerobic soil (pH 5.7, 25ºC)	P-2 and Pm-5-labeled flazasulfuron	One soil (sandy loam) Half-life 14.3 d (water) 20.3 d Sediment 16.5 d entire system	DTPU, DTPP, TPSA, HTPP	DTPU, DTPP and TPSA are known to be products of hydrolysis. It is speculated that degradation initiated with hydrolysis, followed by transformation of hydrolytic products. DTPP transformed to HTPP under anaerobic conditions. ADMP was identified as a minor transformation product formed under anaerobic soil conditions.	2551385 EPA: 47939913
Biotransformation in aerobic water (water pH 6.6-7.7, sediment pH 5.8-7.2, 20ºC)	P-2-labeled flazasulfuron	Two water/sediment systems Half-life 14-15 d water 24 d entire system	DTPU, HTPP	DTPU is known to be the product of hydrolysis. It is speculated that degradation initiated with hydrolysis, followed by biotransformation of hydrolytic products. TPSA was detected as a minor transformation product. DTPP transformed to HTPP.	2551386 EPA: 46220954
Biotransformation in anaerobic water (water pH 9.4, sediment pH 7.1, 25°C)	P-2 and Pm-5-labeled flazasulfuron	Pond water sandy loam sediment Half-life 4.8 d (water) 8.0 d (sediment) 5.2 d (entire system), using kinetics tool PestDF	DTPU, HTPP, 2,3 GTF	It is speculated that degradation initiated with hydrolysis, followed by transformation of hydrolytic products. DTPP, TPSA and ADMP were detected as minor transformation products. DTPP transformed to HTPP. DTPP or HTPP transformed to 2,3 GTF.	2551389 EPA: 46220953

Property	Test substance	Value	Major Transformation Products	Comments	PMRA# and EPA MRID
Mobility					
Adsorption / desorption in soil	^{14}C-flazasulfuron and transformation products, DTPU, DTPP, TPSA ADMP	Soil (pH range 5.5-8.5) Koc range Flazasulfuron: 43.28-157.9 DTPU: 85-222.1 DTPP: 143.1-2616 TPSA: 21.14-43.28 ADMP: 93.5-1017 using PMRA Sorption ToolV2.xlsm		Mobility Flazasulfuron: Medium-very high DTPU:Medium.-high DTPP:Low -medium TPSA:Very high ADMP:Low-high	2551393/2551395 EPA: 46930001/46030002
Soil leaching- aged soil	P-2 and Pm-5-labeled flazasulfuron	Soil section (cm) = % flazasulfuron 0-10= 37-42 10-20= 6-11 20-30= 9-8 Leachate=6-12	Soil section (cm) = % TP **DTPU** 0-10= 12-14 10-20= 2-4 20-30= 2 Leachate=0.1-0.3 **TPSA** 0-10= 5 10-20= 1 20-30= 2.1 Leachate=0.4 **ADMP** 0-10= 5 10-20= 0 20-30= 0.2 Leachate=0.1	Flazasulfuron and its major transformation products have the potential for leaching into ground water.	2551396 EPA: 46220955
Volatilization				Based on vapor pressure (<1.33 x10^{-5} Pa) and Henry's law constant (2.55 × 10^{-11} Pa·m^3·mol^{-1}), volatilization of flazasulfuron from soil or water in the air is not expected.	
Field studies					
Field dissipation	Flazasulfuron	Half-life (day) Oklahoma: 4[a] New York: 5[a] using kinetics tool PestDF Georgia: 5[b] Texas: 7[b] California: 4[b] At face value[c]	DTPU, DTPP, TPSA, ADMP Half-life (day) TPSA: 532 DTPP: 47 using kinetics tool PestDF	Flazasulfuron is not persistent. TPSA is persistent DTPP is moderately persistent	2551262/2551268 EPA: 46220957/47939911
Field leaching				Flazasulfuron and its transformation products were not detected above the LOD (1.2 ppb) in soil below the 30- cm soil depth, after 88 posttreatment.	
Bioaccumulation	Flazasulfuron			Based on Log K_{OW} of 1.30, bioaccumulation is	

Property	Test substance	Value	Major Transformation Products	Comments	PMRA# and EPA MRID
				not expected.	

[a] Sites that are in a Canadian relevant eco-region.
[b] Sites that are not relevant to the Canadian eco-region. The studies were not reviewed by PMRA.
[c]At face value = The reported values are taken from the USEPA DERs.

Table 9 Flazasulfuron Toxicity Profile for Terrestrial Organisms

Organism	Test substance	Endpoint value	Effects	PMRA#	Foreign Reviews
Invertebrates					
Earthworm *Eisenia foetida*	SL-160 (TGAI) (96.2% a.i.)	LC_{50} >15.75 mg a.i./kg soil) NOEC = 15.75 mg a.i./kg soil	Practically non- toxic No adverse effect at the highest dose tested	2551400	USEPA: 2551401 EU: 2716800
	DTPU, DTPP, TPSA, ADMP, HTPP (individually)	LC_{50}> 1250 mg a.i./kg soil	Non-toxic	Not reviewed by PMRA	EU: 2716800
Honey Bee (*Apis mellifera*)	SL-160 (96.3%)	Acute oral LD_{50} > 100 µg a.i./bee NOEC = 100 µg a.i./bee	Non-toxic No adverse effect at the dose tested (limit test)	2551402	USEPA: 2551408 EU: 2716800
	SL-160 (96.3%)	Acute contact LD_{50} > 100 µg a.i./bee NOEC= 100 µg a.i./bee	Non-toxic No adverse effect at the dose tested (limit test)	2551402	USEPA: 2551408 EU: 2716800
	EP-SL-160 25WG (contains 26.3 % w/w a. i.)	Chronic oral LD_{50} > 59.2 µg a.i./bee/day NOED ≥ 59.2 µg a.i./bee/day	Non-toxic No adverse effect at the dose tested (limit test)	2551404	EU: 2716802
	EP-SL-160 25WG (contains 26.3 % w/w a. i.)	Acute larval LD_{50} > 100 µg a.i./larva NOED = 25 µg a.i./larva	2.8 - 44.4% mortality (lowest - highest dose (3.1-100 µg a.i./larva)	2551403	EU: 2716802
Bumble bee	SL-16 (98.5% w/w)	Acute Oral LD_{50} (48 h) > 97.5 µg a.i./bumblebee Acute contact LD50 (48 h) > 100 µg a.i./bumblebee	No sub-lethal effects observed.	Not reviewed by PMRA	EU: 2716802
Non-target arthropod other than bee					
Carabid ground beetle (*Poecilus cupreus*)	SL-160 (95.7% w/w)	LR_{50} > 50 g a.i./ha	Non-toxic No effects in mortality, behaviour or food consumption	2551406	EU: 2716800
Spiders (*Pardosa sp.*)	SL-160 (95.7% w/w)	LR_{50} > 50 g a.i./ha	Non-toxic No effects in mortality, behaviour or food consumption	2551407	EU: 2716800
Birds					
Bobwhite quail (*Colinus virginianus*)	SL-160 (96.3% w/w)	Acute oral LD_{50} >2000 mg a.i./kg bw NOEL = 2000 mg a.i./kg bw	Non-toxic No adverse effect at the highest dose tested	2551439	USEPA: 2551440

Organism	Test substance	Endpoint value	Effects	PMRA#	Foreign Reviews
	SL-160	Acute dietary LC_{50} >5589 ppm NOEC: 5589 ppm LOEC: > 5589ppm	Non-toxic No adverse effect at the highest dose tested	2551444	USEPA: 2551445
	SL-160	Reproductive NOEC =484 ppm LOEC = 1003ppm	Adverse reproductive effects on hatching survival, hatchling weight, and adult male weight gain.	2551448	USEPA: 2551449
Mallard duck (*Anas platyrhynchos*)	SL-160	Acute oral LD_{50} >2250 mg a.i./kg bw NOEL = 1350 mg a.i./kg bw LOEL = 2250 mg a.i./kg bw (♂body weight gains)	Non-toxic NOEL is based on effects on body weight changes in males.	2551441	USEPA: 2551442
	SL-160	Acute dietary LC_{50} >5589 ppm NOEC: 5589 ppm LOEC: >5589 ppm	Non-toxic No adverse effect at the highest dose tested	2551446	USEPA: 2551447
	SL-160	Reproductive NOEC =1003 ppm. LOEC >1003 ppm	No adverse effect at the highest dose tested	2551451	USEPA: 2551452
Zebra Finch	SL-160	Acute oral LD_{50} >2000 mg a.i./kg bw	Practically nontoxic	2551443	USEPA DER not submitted to PMRA
Mammals					
Laboratory Rat	SL-160	Acute oral LD_{50} > 5000 mg a.i./kg bw	Low toxicity	2551311	USEPA: 2551312
	EP - SL-160 25% WG (26.9%)	Oral LD50: ♂ = 4694, ♀ = 4908 mg product/kg bw	Low toxicity	2551237	USEPA: 2551237
	SL-160	Dermal LD_{50} > 2000 mg a.i./kg bw	Low toxicity	2551313	USEPA: 2551314
	SL-160	90-day dietary, NOAEL = 1000 ppm (♂ = 57.1, ♀ = 61.5 mg/kg bw/d)) LOAEL = 5000 ppm (♂ = 287, ♀ = 309 mg/kg bw/d)	Effects at LOAEL: ↓ bw & bwg, ↑ wts of liver and kidneys; kidney focal tubular atrophy & dilatation of proximal tubules (♂); ↓ food intake & food efficiency (♀)	2551323	USEPA: 2551324
	SL-160	2-Generation dietary reproductive **Parental toxicity** NOAEL: ♂ = 200 ppm (13.7 mg/kg bw/d), ♀ = 2000 ppm (155 mg/kg bw/d) LOAEL: ♂ = 2000 ppm (155 mg/kg bw/d); ♀ = 10000 ppm (760 mg/kg bw/d) **Reproductive toxicity:** NOAEL = 2000 ppm (♂ = 135, ♀ = 155 mg/kg bw/d) LOAEL = 10000 ppm (♀ = 760 mg/kg bw/d) **Offspring toxicity:** NOAEL = 2000 ppm	**Parental toxicity:** Effects at LOAEL: ↓ bw, food; kidney pathology - enlargement, discolouration, dilated renal pelvis, granularity, nephropathy, and tubular dilatation (♂) **Reproductive toxicity:** based on ↓ birth wt at 2nd generation **Offspring toxicity:** Effects at LOAEL: ↓ pup wts in both generations	2551336	USEPA: 2551337

Organism	Test substance	Endpoint value	Effects	PMRA#	Foreign Reviews
		(♂ = 134.8, ♀ = 155.0 mg/kg bw/d) LOAEL = 10000 ppm (♂ = 674.6, ♀ = 760.2 mg/kg bw/d)			
Vascular plants					
10 species	EP-SL-160 24.99% WG	**Seedling emergence** **Monocot** EC_{25} = 2.94 g a.i./ha NOAEC= 0.195 g a.i./ha (Ryegrass – dry weight) **Dicot** EC_{25} =1.2 g a.i./ha NOAEC <0.195g a.i./ha (Cabbage)	Phytotoxic effects included decrease in leaf size, chlorosis, reduced growth	2551468/2726193	USEPA: 2551469
10 species	EP-SL-160 25% WG	**Vegetative vigor** **Monocot** EC_{25} =0. 46 g a.i./ha NOEC: 0.391 g a.i./ha (Ryegrass- dry weight) **Dicot** EC_{25} = 0.045 g a.i./ha NOEC: 0.24 g a.i./ha (radish- plant height) **HC_5 = 0.137 g a.i./ha**	Phytotoxic effects included necrosis, chlorosis, leaf cupping, buggy whip (corn shoot tips may also fail to unroll or unfurl from the coleoptiles), discoloration, reduced tillers, crinkled leaves and purple veins.	2551470	USEPA: 2733075

Table 10 Screening Level Risk Assessment For Terrestrial Organisms Other Than Birds, Mammals and Honey Bees

Organism	Test Substance	Endpoint/ Uncertainity factor	Assessment Endpoint	EEC mg a.i./kg soil	RQ	LOC exceeded?
Soil Invertebrates						
Earthworm	SL-160	LC50= >15.75 (mg a.i./kg soil) /2	> 7.875	0.0222	< 0.0028	No
		NOEC = 15.75(mg a.i./kg soil) /1	15.75	0.0222	0.0014	No
Terrestrial Invertebrates						
Spider	SL-160	LR50 = > 50(mg a.i./kg) /1	> 50	0.0222	< 0.0004	No
Canabid beetle	SL-160	LR50= > 50(mg a.i./kg)/1	> 50	0.0222	<0.0004	No
Terrestrial Plants						
Seedling Emergence						
Cabbage	SL-160	EC25= 1.2(mg a.i./kg) /1	1.2	0.0222	0.0185	No
Ryegrass	SL-160	EC25 = 2.94(mg a.i./kg) /1	2.94	0.0222	0.008	No
Vegetative Vigor - Cumm App rate on leaf (g a.i./ha)						

Organism	Test Substance	Endpoint/ Uncertainity factor	Assessment Endpoint	EEC mg a.i./kg soil	RQ	LOC exceeded?
Radish	SL-160	EC25 = 0.045(g a.i./ha) /1	0.045	50	**1111**	Yes
Ryegrass	SL-160	EC25 = 0.46 (g a.i./ha) /1	0.46	50	**108.7**	Yes
All plant tested	SL-160	HC_5 = 0.137(g a.i./ha)/1	0.137	50	**364.96**	Yes

Table 11 Screening Level Risk Assessment for Pollinators

Foliar Spray Application at rate 0.05 kg a.i./ha					
	EEC (µg a.i./g)	Exposure to bee (µg a.i./bee/day)	Endpoint value	RQ	LOC exceeded?
Adult acute contact	4.9	0.12	100 µg a.i./bee	0.001	No
Adult acute oral	4.9	1.4308	100 µg a.i./bee	0.014	No
Adult chronic oral	4.9	1.4308	59.2 µg a.i./bee	0.024	No
Larvae acute oral	4.9	0.6076	100 µg a.i./bee	0.006	No

Assume the larval endpoint applies for worker, drone and queen larvae
Assume the adult bee endpoint applies for drones and queens.
Food consumption rate for larvae is assumed to be 124 mg/day/larva
LOC = 0.4 for acute and 1 for chronic

Table 12 Screening Level Risk Assessments to Birds and Wild Mammals

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	On-field EDE[1] (mg a.i./kg bw)	On-field RQ	LOC exceeded?
Flazasulfuron use pattern: 1 × 50 g a.i./ha. Ground Boom Sprayer Medium					
Birds					
Small Bird (0.02 kg)					
Acute	200.00	Insectivore	4.07	0.02	No
Reproduction	47.750	Insectivore	4.07	0.09	No
Medium Sized Bird (0.1 kg)					
Acute	200.00	Insectivore	3.18	0.02	No
Reproduction	47.750	Insectivore	3.18	0.07	No
Large Sized Bird (1 kg)					
Acute	200.00	Herbivore (short grass)	2.05	0.01	No
Reproduction	47.750	Herbivore (short grass)	2.05	0.04	No

	Toxicity (mg a.i./kg bw/d)	Feeding Guild (food item)	On-field EDE[1] (mg a.i./kg bw)	On-field RQ	LOC exceeded?
Mammals					
Small Size Mammal (0.015 kg)					
Acute	469.40	Insectivore	2.34	0.005	No
Reproduction	13.70	Insectivore	2.34	0.171	No
Medium Sized Mammal (0.035 kg)					
Acute	469.40	Herbivore (short grass)	4.54	0.01	No
Reproduction	13.70	Herbivore (short grass)	4.54	0.33	No
Large Sized Mammal (1 kg)					
Acute	469.40	Herbivore (short grass)	2.43	0.01	No
Reproduction	13.70	Herbivore (short grass)	2.43	0.18	No

[1] EDE = Estimated daily exposure; is calculated using the following formula: (FIR/BW) × EEC, where:
FIR: Food Ingestion Rate (Nagy, 1987).
For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used;
for generic birds with body weight greater than 200 g, the "all birds" equation was used:
Passerine Equation (body weight < or =200 g): FIR (g dry weight/day) = 0.398(BW in g) $^{0.850}$
All birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g) 0.651.
For mammals, the "all mammals" equation was used: FIR (g dry weight/day) = 0.235(BW in g) 0.822
BW: Generic Body Weight
EEC: Concentration of pesticide on food item based on Hoerger and Kenaga (1972) and Kenaga (1973)
and modified according to Fletcher *et al*. (1994).
At the screening level, relevant food items representing the most conservative EEC for each feeding guild are used.

Table 13 Species Sensitivity Distribution (SSDs) analysis presenting HC_5 values for Flazasulfuron 25WG Herbicide

Test material	Exposure	Endpoint (g a.i./ha)	Terrestrial Plants (Vegetative Vigour) (g a.i./ha)
EUP	Acute	EC_{50}	HC_5: 0.137
			CI: 0.038-0.265; FA: 0.4-23%

EUP = end-use product
CI = lower and upper confidence level of HC_5 (0.038 = lower level of HC_5 and 0.265 = upper level of HC_5)
FA = fraction of species (0.4% = lower level fraction affected and 23% upper level fraction affected)

Table 14 Refined risk assessment of flazasulfuron with spray drift scenario

Organism Class	Organism	Endpoint / Uncertainty Factor	Assessment Endpoint	One application of 50 g a.i./ha				LOC Exceeded?
				EEC	6% EEC	On-field RQ	Off-field RQ (6% drift)	
Terrestrial plants	All plant species tested– based on HC_5 of SSD	HC5/1	0.137 g a.i./ha	50[a]	3	365	22	Yes
Freshwater plants and algae	Green algae	EC50/ 2	0.00205 mg a.i./L	0.006[b]	0.0004	3	0.2	No
				0.033[c]	0.002	16	1	Yes
	Lemna	EC50/2	0.00002 mg a.i./L	0.006[b]	0.0004	313	20	Yes

[a]Cumm App rate on leaf (g a.i./ha)
[b]EEC water 80 cm (mg a.i./L)
[C]EEC water 15 cm (mg a.i./L)

Table 15 Screening level risk assessment for aquatic organisms (Scenario 1: 80-cm water depth)

Organism	Test Substance	Endpoint/Uncertainity factor	Assessment Endpoint	EEC mg a.i./L water (80-cm water depth)	RQ	LOC exceeded?
Freshwater Invertebrates						
Daphnia	SL-160	EC50= >106 mg a.i./L /2	> 53	0.006	<0.0001	No
	DTPU	EC50 = >178 mg a.i./L /2	> 89	0.053	<0.00006	No
	DTPP	EC50 = 166 mg a.i./L /2	83	0.005	0.000056	No
	TPSA	EC50 = 60.2 mg a.i./L /2	30.1	0.004	0.0001	No
	ADMP	EC50 = >100 mg a.i./L/2	> 50	0.003	<0.00005	No
	SL-160	NOEC = 6.39 mg a.i./L/1	6.39	0.006	0.00098	No
Midge	SL-160	NOEC = > 0.1 mg a.i./L /1	> 0.1	0.006	<0.6	No
	DTPU	LC50 = > 100 mg/L/ 2	> 50	0.005	<0.0001	No
	HTPP	LC50 = > 100 mg/L/ 2	> 50	0.004	<0.00009	No
Freshwater Fish						
Rainbow	SL-160	LC50 = 120 mg a.i./L /10	12	0.006	0.0005	No
Bluegill	SL-160	LC50 = >98 mg/L /10	> 9.8	0.006	<0.0006	No
Rainbow	DTPU	LC50= >82 mg a.i./L /10	> 8.2	0.005	<0.0006	No
	DTPP	LC50 = >82 mg a.i./L /10	> 8.2	0.0046	<0.00056	No
	TPSA	LC50 = >100 mg a.i./L /10	> 10	0.0035	<0.0003	No
	ADMP	LC50 = >100 mg a.i./L /10	> 10	0.002	<0.0002	No

Organism	Test Substance	Endpoint/Uncertainity factor	Assessment Endpoint	EEC mg a.i./L water (80-cm water depth)	RQ	LOC exceeded?
	SL-160	NOEC = 5 mg a.i./L/1	5	0.006	0.001	No
	SL-160	NOEC (EL) = 17 mg a.i./L/1	17	0.006	0.00036	No
Zebra Fish	DTPU	LC50 = 105.7 mg a.i./L /10	10.57	0.005	0.0005	No
	DTPP	LC50 = 133.5 mg a.i./L/ /10	13.35	0.0046	0.0003	No
Freshwater Algae						
Green algae	SL-160	EC50 = 0.0041 mg a.i./L /2	0.00205	0.006	**3.05**	Yes
Diatom	SL-160	EC50 = 7.2 mg a.i./L /2	3.6	0.006	0.002	No
Blue-green algae	SL-160	EC50 = >9.3 mg a.i./L /2	> 4.65	0.006	<0.001	No
Green algae	DTPU	EC50 = 9.1 mg a.i./L /2	4.5	0.005	0.001	No
	DTPP	EC50 = 37 mg a.i./L /2	18.5	0.005	0.0002	No
Freshwater Vascular Plant						
Lemna	SL-160	EC50 = 0.00004 mg a.i./L /2	0.00002	0.006	**312.5**	Yes
Saltwater Invertebrates						
Mysid shrimp	SL-160	LC50 = 107 mg a.i./L /2	53.5	0.006	0.0001	No
Eastern oyster	SL-160	LC50 = >116 mg a.i./L /2	> 58	0.006	<0.0001	No
Saltwater Fish						
Sheepshead minnow	SL-160	LC50 = >140 mg a.i./L /10	> 14	0.006	<0.0004	No
Saltwater Algae						
Diatom	SL-160	EC50 = >7.4 mg a.i./L/2	> 3.7	0.006	<0.0016	No

Table 16 Screening level risk assessment for aquatic organisms (Scenario 2: 15-cm water depth)

Organism	Test Substance	Endpoint/Uncertainity factor	Assessment Endpoint	EEC mg a.i./L water (15-cm water depth)	RQ	LOC exceeded?
Freshwater Invertebrates						
Daphnia	SL-160	EC50 /2	> 53	0.033	<0.0006	No
	DTPU	EC50 /2	> 89	0.03	<0.003	No
	DTPP	EC50 /2	83	0.025	0.0003	No
	TPSA	EC50 /2	30.1	0.019	0.0006	No
	ADMP	EC50 /2	> 50	0.013	<0.0003	No
	SL-160	NOEC/1	6.39	0.033	0.005	No
Midge	SL-160	NOEC /1	> 0.1	0.033	<0.33	No
	DTPU	NOEC /1	> 100	0.03	<0.0006	No
	HTPP	NOEC /1	> 100	0.023	<0.00005	No
Freshwater Fish						
Rainbow	SL-160	LC50 /10	12	0.033	0.003	No
Bluegill	SL-160	LC50 /10	> 9.8	0.033	<0.003	No
Rainbow	DTPU	LC50 /10	> 8.2	0.03	<0.003	No
	DTPP	LC50 /10	> 8.2	0.025	<0.0029	No
	TPSA	LC50 /10	> 10	0.019	<0.0019	No
	ADMP	LC50 /10	> 10	0.013	<0.0013	No
	SL-160	NOEC	5	0.033	0.007	No
	SL-160	NOEC (EL)	17	0.033	0.002	No
Zebra Fish	DTPU	LC50 /10	10.57	0.03	0.003	No
	DTPP	LC50 /10	13.35	0.025	0.002	No
Amphibians						
	SL-160	LC50 /10	12	0.033	0.003	No
	SL-160	NOEC	5	0.033	0.007	No

Organism	Test Substance	Endpoint/Uncertainity factor	Assessment Endpoint	EEC mg a.i./L water (15-cm water depth)	RQ	LOC exceeded?
	SL-160	NOEC (EL)	17	0.033	0.002	No
Freshwater Algae						
Green algae	SL-160	EC50 /2	0.00205	0.033	**16.3**	Yes
Diatom	SL-160	EC50 /2	3.6	0.033	0.009	No
Blue-green algae	SL-160	EC50 /2	> 4.65	0.033	<0.007	No
Green algae	DTPU	EC50 /2	4.5	0.028	0.006	No
	DTPP	EC50 /2	18.5	0.024	0.001	No

Table 17 Level 1 aquatic ecoscenario modelling EECs (µg a.i./L) for flazasulfuron in a water body 0.8 m deep, excluding spray drift.

EEC (µg a.i./L)								
Region	**Peak**	**96 hr**	**21 d**	**60 d**	**90 d**	**Yearly**	**Peak (in pore water)**	**21-day (in pore water)**
Rate: 1 × 50 g a.i./ha								
BC	0.12	0.12	0.12	0.12	0.12	0.056	0.04	0.04
Prairie	1.4	1.3	1.3	1.2	1.2	0.59	0.46	0.46
ON	**1.7**	**1.6**	**1.5**	**1.5**	**1.4**	**0.69**	**0.56**	**0.56**
QC	0.57	0.56	0.53	0.46	0.43	0.23	0.18	0.18
Atlantic	1.1	1.1	1.1	1.2	1.2	0.503	0.51	0.51

Table 18 Refined risk assessments determined for run-off of flazasulfuron in a water body

Organism (exposure)	Endpoint value	EEC (µg a.i./L) – Peak value and region*	RQ	LOC exceeded?
80 cm water body				
Lemna	EC_{50}/2 = 0.02 µg a.i./L	0.12 µg a.i./L (BC)	6	Yes
		1.4 µg a.i./L (Prairies)	70	Yes
		1.7 µg a.i./L (ON)	85	Yes
		0.57 µg a.i./L (QC)	28.5	Yes
		1.1 µg a.i./L (Atlantic)	55	Yes

Table 19 Registered Alternatives

Active ingredients	EP examples (Registration Number)	Group	Spectrum of activity
Grapes			
Dichlobenil	Casoron G-4 (12533)	20	Pre-emergent weed control
Napropamide	Devrinol 2-XT (31688)	15	Pre-emergent weed control
Diuron	Karmex (28543)	7	Pre-emergent weed control
Dimethenamid	Frontier Max (29194)	15	Pre-emergent weed control
Flumioxazin	Flumioxazin 51 (29235)	14	Pre-emergent weed control
Simazine	Princep Nine-T (16370)	5	Pre-emergent weed control
Sethoxydim	Poast Ultra (24835)	1	Postemergent control of grasses
Fluazifop-p-butyl	Venture L (21209)	1	Postemergent control of grasses
Carfentrazone	Aim EC (28573)	14	Pre-emergent control of broadleaf weeds
Glyphosate	Roundup Transorb (28198)	9	Postemergent weed control
Paraquat ion	Gramoxone (8661)	22	Postemergent weed control
Glufosinate	Ignite SN (28532)	10	Postemergent weed control

Active ingredients	EP examples (Registration Number)	Group	Spectrum of activity
Woody conifer ornamentals, forestry conifer release, and Christmas trees			
Propyzamide	Kerb (30264)	15	Pre- and postemergent control of grasses
s-metolachlor	Dual II Magnum (25729)	15	Pre- and postemergent weed control
Flumioxazin	Flumioxazin 51 (29235)	14	Pre-emergent weed control
Isoxaben	Gallery (24110)	21	Pre-emergent control of broadleaf weeds
Dichlobenil	Casoron G-4 (12533)	20	Pre-emergent weed control
Chlorthal	Dacthal W-75 (8963)	3	Pre-emergent weed control
Napropamide	Devrinol 2-XT (31688)	15	Pre-emergent weed control
Simazine	Princep Nine-T (16370)	5	Pre-emergent weed control
Pendimethalin	Prowl H_2O (29542)	3	Pre-emergent weed control
Trifluralin	Treflan EC (23933)	3	Pre-emergent weed control
Fluazifop-p-butyl	Venture L (21209)	1	Postemergent control of grasses
Oxyfluorfen	Goal 2XL (24913)	14	Postemergent control of broadleaf weeds
Glyphosate	VisionMax (27736)	9	Postemergent weed control
Clopyralid	Lontrel 72 (31039)	4	Postemergent control of broadleaf weeds
Hexazinone	Velpar DF (31766)	5	Pre- and postemergent weed control
Bare ground and non-crop areas			
2,4-D amine	2,4-D Amine (28271)	4	Postemergent control of broadleaf weeds
Aminopyralid	Milestone (28517)	4	Postemergent control of broadleaf weeds
Metsulfuron-methyl	Escort (23005)	2	Postemergent control of broadleaf weeds
Chlorsulfuron	Telar XP (30036)	2	Postemergent control of broadleaf weeds
Triclopyr	Garlon Ultra (28434)	4	Postemergent control of woody plants and weeds
Clopyralid	Lontrel 360 (23545)	4	Postemergent control of broadleaf weeds
Diuron	Karmex (28543)	7	Pre-emergent weed control
Glyphosate	Roundup Transorb (28198)	9	Postemergent weed control
Bromacil	Hyvar X-L (11018)	5	Pre- and postemergent weed control

Table 20 List of Supported Uses

Items	Label claims that are supported
Application rates	Pre- and post-emergence applications at 150-200 g/ha (i.e., 37.5-50 g a.i./ha).
Adjuvants	For post-emergence application, a NIS at 0.25% v/v or a COC or MSO at 1.0% v/v is required.
Efficacy claims	Pre-emergent control of annual bluegrass, hare barley, creeping bentgrass, downy brome, fescue (rough, sheep, and tall), foxtail (giant, green, and yellow), Italian ryegrass, field sandbur, California burclover, chickweed (common and mouse-ear), crimson clover, dandelion, redstem filaree, hairy fleabane, geranium Carolina, groundsel, henbit, lamb's-quarters, mallow (common and little), mustard (Indian and wild), pigweed (prostrate, redroot, and tumble), common purslane, common ragweed, shepherd's-purse, annual sow-thistle, corn speedwell, spurge (creeping, prostrate, and spotted), panicle willoweed, and yellow nutsedge. Pre-emergent suppression of large crabgrass, witchgrass, horseweed (Canada and mare's-tail), oxtongue bristly, and sow-thistle. Post-emergent control of all weeds listed above (except hare barley) plus crabgrass (large and smooth), catchweed bedstraw, wild carrot, mayweed chamomile, clover (hop and large hop), horseweed (Canada and mare's tail), field pansy, field pepperweed, thistle (bull and Canada), and chickweed wintergreen. Post-emergent suppression of rabbitfoot polypogon, witchgrass, hare barley, dandelion, rough fleabane, and oxtongue bristly.
Hosts and use sites	Grapes, conifer trees, and industrial vegetation management sites.
Application	Grapes: Apply as a directed spray to grape vines established for at least three years. Use of a

Items	Label claims that are supported
methods and timing	protective sleeve is required for the 3rd year vines to minimize injury potential. Conifer Trees: Apply over-the-top to conifers, which are established for more than a year, prior to spring bud break or when conifers are sufficiently hardened off. Directed applications are recommended to reduce phytotoxicity potential as well as to conifers that have new growth or are not sufficiently hardened off. Do not apply to conifer seedbeds or trees within 1 year of seeding. Industrial Vegetation Management: Apply after weeds have broken dormancy. Best results are obtained if weeds are small or 1 to 2 weeks after mowing.
Tank-mixtures	Grapes: For improved burndown weed control, tank mix with Ignite SN or Ignite 15SN or glyphosate herbicides, which are labelled for the same use pattern. For longer residual weed control, tank mix with Karmex XP, Karmex DF, Diurex 80W, Alligare Diuron 80WDG, Simadex Simazine Flowable, Princep Nine-T, or Simazine 480. Conifer Trees: For improved post-emergent weed control, tank mix with glyphosate while for longer residual weed control, tank mix with another residual herbicide labelled for use in conifer trees. Industrial Vegetation Management: For improved post-emergence weed control, tank mix with glyphosate.

Table 21 Toxic Substances Management Policy considerations – comparison to TSMP Track 1 Criteria

Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria				
TSMP Track 1 Criteria	**TSMP Track 1 Criterion value**		**Flazasulfuron Endpoints**	**Comments**
CEPA toxic or CEPA toxic equivalent[1]	Yes			
Predominantly anthropogenic[2]	Yes			
Persistence[3]	Soil	Half-life ≥ 182 days	Half-life: 12-124 days (laboratory); 4-7 days (field studies)	
	Water	Half-life ≥ 182 days	Half-life: 15 days	
	Sediment	Half-life ≥ 365 days	Total system Half-life: 24 days	
	Air	Half-life ≥ 2 days or evidence of long range transport	Volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (<1.33 x10^{-5} Pa) and Henry's Law Constant (2.55 × 10^{-11} Pa·m^3·mol^{-1}).	
Bioaccumulation[4]	Log K_{OW} ≥ 5		1.30	
	BCF ≥ 5000		not available	
	BAF ≥ 5000		not available	
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.	

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e., all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Field data (e.g., BAFs) are preferred over laboratory data (e.g., BCFs) which, in turn, are preferred over chemical properties (e.g., log K_{OW}).

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

The MRL proposed for flazasulfuron in Canada is the same as the corresponding tolerance in the United States.

Currently, there are no Codex MRLs[9] listed for flazasulfuron in or on any commodity on the Codex Alimentarius Pesticide Residues in Food and Feed website.

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.

[9] The Codex Alimentarius Commission is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

References

A. List of Studies/Information Submitted by Registrant

PMRA Document Number	References

1.0 Chemistry

2551289	2004, Product Chemistry Stuides For Technical Flazasulfuron (SL-160) - Series 61, DACO: 2.11.1, 2.11.2, 2.11.3, 2.11.4 CBI
2679805	2016, Flazasulfuron (SL-160) Technical, Five-Batch Analysis, DACO: 2.13.2, 2.13.3 CBI
2679804	2016, Characterization of [CBI removed] Reference Substance, Validation of Analytical Methodology for Quantitation of [CBI removed] in SL-160, and Analysis of Five (5) Batches of SL-160 (Flazasulfuron), DACO: 2.11.4, 2.12, 2.13 CBI
2551301	1993, Flazasulfuron (SL-160) - Color, Physical State, Odor, Melting Point, Bulk Density, Oxidation-Reduction, Impact Explodability, DACO: 2.14.1, 2.14.2, 2.14.3, 2.14.4, 2.14.6
2551302	1992, Flazasulfuron (SL-160) - Dissociation Constant, DACO: 2.14.10
2551303	1994, Flazasulfuron (SL-160) - Octanolavater Partition Coefficient, DACO: 2.14.11
2551308	1994, Flazasulfuron (SL-160) - Solubility, DACO: 2.14.7, 2.14.8
2551309	1993, Flazasulfuron (SL-160) - Vapor Pressure, DACO: 2.14.9
2551304	2007, UV Spectra of SL-160 and Degradates, ADMP, DTPP, and DTPU, DACO: 2.14.12
2551307	1993, SL-160 - pH, DACO: 2.14.15
2551305	2004, SL-160 (Flazasulfuron) TGAI- Stability to Normal and Elevated Temperature, Metals, and Metal Ions, DACO: 2.14.13
2551306	1994, Flazasulfuron (SL-160) - Storage Stability, DACO: 2.14.14
2551233	2004, Product Chemistry Studies For Flazasulfuron 25WG, DACO: 3.2.1, 3.2.2, 3.2.3 CBI
2551234	2004, Product Chemistry Studies For Flazasulfuron 25WG - SERIES 62 -, DACO: 3.3.1, 3.4, 3.4.1 CBI
2551235	1996, Product Chemistry Studies For Flazasulfuron 25WG - SERIES 63 -, DACO: 3.5.1, 3.5.10, 3.5.11, 3.5.12, 3.5.13, 3.5.14, 3.5.15, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.8, 3.5.9
2551367	2004, Independent Laboratory Validation (ILV) of CCRL'S Method (CCRL-MTH-045) for the Analysis of SL-160 and Its Metabolites (TPSA, DTPU, DTPP, and ADMP) in Soil, DACO: 8.2.2.1
2551370	2014, Validation of Method GPL-MTH-082: Analytical Method for the Determination of SL-160 and its Metabolites DTPU, DTPP, and TPSA in Water by LC-MS/MS, DACO: 8.2.2.3
2551371	2014, Independent Laboratory Validation of Ishihara Sangyo Kaisha (ISK) Analytical Method for the Determination of SL-160 and Its Metabolites DTPU, DTPP, and TPSA in Surface and Drinking Water by LC-MS/MS (Document

Number: GPL-MTH-082), DACO: 8.2.2.3
2551372 1996, Analytical Procedure for the Determination of Flazasulfuron (SL-160) Residues in Animal Tissues and Human Fluids, DACO: 8.2.2.4

2.0 Human and Animal Health

2551355 1994, Study to evaluate the distribution and excretion of 14C-SL-160(P) in rats, DACO: 4.5.9
2551356 1994, Study to evaluate the distribution and excretion of 14C-SL-160(P) following repeated administration of SL-160 in rats, DACO: 4.5.9
2551357 1995, Study to evaluate the distribution and excretion of 14C-SL-160(Pm) in rats, DACO: 4.5.9
2551358 1995, Study to evaluate the pharmacokinetics of 14C-SL-160(P) in the blood of rats, DACO: 4.5.9
2551359 1995, Study to evaluate the pharmacokinetics of 14C-SL-160(Pm) in the blood of rats, DACO: 4.5.9
2551360 1995, Study of the biliary excretion of radiolabel following oral administration of 14C-SL-160(Pm) to Sprague-Dawley rats, DACO: 4.5.9
2551361 1995, Study to evaluate the distribution and excretion of 14C-SL-160(Pm) following repeated administration of SL-160 in rats, DACO: 4.5.9
2551362 1995, Study of the biliary excretion of radiolabel following oral administration of 14C-SL-160(P) to Sprague-Dawley rats, DACO: 4.5.9
2551363 1995, Study to identify and characterize the metabolites of [14C]-SL-160, DACO: 4.5.9
2551311 1988, SL-160 Technical: Acute Oral Toxicity Study in Rats, DACO: 4.2.1
2551313 1988, SL-160 Technical: Acute Dermal Toxicity Study in Rats, DACO: 4.2.2
2551315 1988, SL-160 Technical: Acute Inhalation Toxicity Study in Rats, DACO: 4.2.3
2551317 1993, Primary eye irritation study in albino rabbits with SL-160, DACO: 4.2.4
2551319 1993, Primary dermal irritation study in albino rabbits with SL-160, DACO: 4.2.5
2551321 1995, Dermal Sensitization Study (Closed-Patch Repeated Insult) in Guinea Pigs with SL-160, DACO: 4.2.6
2551323 1988, SL-160 technical: 13-Week oral subchronic toxicity study in rats, DACO: 4.3.1
2551325 1994, SL-160 technical: 13-Week oral subchronic toxicity study in dogs, DACO: 4.3.2
2694935 1995, SI-160 technical; 2-Week oral (gavage) study in rats, DACO: 4.3.8
2551327 1995, SL-160 technical: 12-Month oral chronic toxicity study in dogs, DACO: 4.3.2
2551329 1994, A 21-day repeated dose dermal toxicity study in albino rabbits with technical SL-160, DACO: 4.3.5
2551331 1995, An oncogenicity study in mice with SL-160, DACO: 4.4.2, 5.5.2
2551333 1995, SL-160 Technical: 24-Month oral chronic toxicity and oncogenicity study in rats, DACO: 4.4.4, 5.5.3
2551336 1995, A two-generation reproduction study in rats with technical SL-160, DACO: 4.5.1
2551343 1996, SL-160 Technical: Developmental Toxicity Study in Rats, DACO: 4.5.2
2551345 1988, Teratogenicity Study in Rabbits with SL-160 Technical, DACO: 4.5.3
2551347 1987, SL-160 Technical: Microbial mutagenicity study, DACO: 4.5.4

2551349 1993, L5178Y TK+/- Mouse lymphoma mutagenesis assay with a confirmatory assay with SL-160, DACO: 4.5.5
2551351 1988, SL-160 Technical: In vitro cytogenetics test, DACO: 4.5.6
2551353 1995, Micronucleus cytogenetic assay in mice with SL-160, DACO: 4.5.7
2551323 2002, A Range-Finding Acute Neurotoxicity Study in Rats with SL-160, DACO: 4.5.12
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B. Additional Information Considered

i) Published Information

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