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Proposed Registration Decision

Mesosulfuron-methyl

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

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Overview

Registration Decision for Mesosulfuron-methyl

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing to grant full registration for the sale and use of Mesosulfuron-methyl Technical Herbicide and Silverado WDG Herbicide containing the technical grade active ingredient Mesosulfuron-methyl, used to control wild oats in spring and durum wheat.

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 Mesosulfuron-methyl Technical Herbicide and Silverado WDG 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 (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of the Health Canada website at healthcanada.gc.ca/pmra.

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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."

What Is Mesosulfuron-methyl?

Silverado WDG Herbicide (containing the active ingredient mesosulfuron-methyl) is a postemergent herbicide (in other words, a herbicide applied after the crop has emerged from the ground). It is applied to spring and durum wheat using ground application equipment to control wild oats.

Silverado WDG herbicide contains the active ingredient mesosulfuron-methyl which belongs to the sulfonylurea family of herbicides and is classified as a Group 2 Herbicide. The primary mode of action of mesosulfuron-methyl is to block the enzyme acetohydroxyacid synthase. Without this enzyme weeds typically die within 4 to 6 weeks after application.

Health Considerations

Can Approved Uses of Mesosulfuron-methyl Affect Human Health?

Mesosulfuron-methyl is unlikely to affect your health when used according to label directions.

Potential exposure to mesosulfuron-methyl may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which 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 mesosulfuron-methyl products are used according to label directions.

The technical grade active ingredient mesosulfuron-methyl was of low acute oral and dermal toxicity and of slight toxicity by the inhalation route in rats. It was not irritating when applied to the skin of the rabbit but was minimally irritating to the rabbit eye. Mesosulfuron-methyl was not a skin sensitizer in the guinea pig.

The formulation Silverado WDG Herbicide, containing 2.26% of the technical active ingredient, mesosulfuron-methyl, was of low acute toxicity via the oral, dermal and inhalation routes. It was minimally irritating to the skin but moderately irritating to the eye of the rabbit. Similar to the active ingredient, it was not a skin sensitizer.

Mesosulfuron-methyl did not cause cancer in animals and did not damage genetic material (DNA). There was also no indication that mesosulfuron-methyl caused damage to the nervous system and there were no adverse effects on the reproduction system. The first signs of toxicity in animals given daily doses of mesosulfuron-methyl over longer periods of time were effects in the stomach. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When mesosulfuron-methyl was given to pregnant animals, no treatment related effects on the developing foetus or the mother were observed up to the limit dose, indicating that the fetus is not more sensitive to mesosulfuron-methyl than the adult animal. Because of this observation, extra protective factors were not warranted for risk assessment.

Residues in Water and Food

Dietary risks from foodand water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants, the subpopulation that would ingest the most mesosulfuron-methyl relative to body weight, are expected to be exposed to less than 1% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from mesosulfuron-methyl is not of concern for all population subgroups. Mesosulfuron-methyl is not carcinogenic; therefore, a cancer dietary exposure assessment is not required.

A single dose of mesosulfuron-methyl is not likely to cause acute health effects in the general population (including infants and children). An acute reference dose was not established; therefore, an acute dietary intake estimate is not required.

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 mesosulfuron-methyl on wheat were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation section of this document.

Occupational Risks From Handling Silverado WDG Herbicide

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

Farmers and pesticide applicators mixing, loading or applying Silverado WDG Herbicide as well as field workers re-entering freshly treated wheat fields can come in direct contact with Silverado WDG Herbicide on the skin or through inhalation of spray mists.

Therefore, the label will specify that anybody who is handling Silverado WDG Herbicide must wear a long-sleeved shirt, long pants, chemical resistant gloves and shoes plus socks during mixing, loading, clean-up and repair. In addition, the label will also specify to wear goggles or face shield during mixing/loading and for applicators to wear long-sleeved shirt, long pants and shoes plus socks.

Taking into consideration these label requirements and that occupational exposure is expected to be short to intermediate term, because this herbicide can only be applied once per season to any given field, risk to farmers, applicators or workers is not a concern.

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

For postapplication, exposure is expected to be minimal since Silverado WDG Herbicide is applied directly to the ground using a groundboom sprayer shortly after it has been planted. Therefore, health risks to workers entering treated fields are not of concern.

Environmental Considerations

What Happens When Mesosulfuron-methyl Is Introduced Into the Environment?

Mesosulfuron-methyl and its transformation products are non-persistent to moderately persistent in the environment (terrestrial and aquatic). The potential of these chemicals to reach groundwater is minimal. Mesosulfuron-methyl is expected to impact terrestrial plants; therefore, buffer zones are needed for the protection of non-target plants.

Mesosulfuron-methyl is transformed by microorganisms in soil and aquatic systems. In soil, mesosulfuron-methyl is non-persistent to moderately persistent and its transformation products are not expected to be persistent. Adsorption studies indicate mesosulfuron-methyl has relatively high soil mobility. However, a field dissipation study did not detect the herbicide below 30 cm. Leaching of mesosulfuron-methyl into groundwater is, therefore, not expected to be a major route of contamination under Canadian wheat growing conditions. This is supported by the results of groundwater modelling scenarios. In aquatic systems, mesosulfuron-methyl is non-persistent to moderately persistent. Mesosulfuron-methyl and its transformation products are unlikely to accumulate in sediments as they transform rapidly under anaerobic conditions.

Mesosulfuron-methyl does not present a risk to earthworms, bees, birds, small mammals, fish, aquatic vascular plants, aquatic invertebrates and algae. As a herbicide, mesosulfuron-methyl poses a risk to non-target terrestrial plants. Precautionary statements are thus included on the end-use product (Silverado WDG Herbicide) label and buffer zones of one metre (terrestrial habitats) are required to mitigate risk to non-target plants from spray drift.

Value Considerations

What Is the Value of Silverado WDG Herbicide?

> **Silverado WDG Herbicide, a postemergence herbicide, controls wild oats in wheat (spring and durum).**
>
> A single application of Silverado WDG Herbicide provides effective control of wild oats in spring and durum wheat. Silverado WDG Herbicide is compatible with integrated weed management practices, conservation tillage, and conventional crop production systems. Silverado WDG Herbicide is applied after weed emergence, allowing growers to better assess whether the herbicide is suitable for the particular weed species present.

Measures to Minimize Risk

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

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

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with Silverado WDG Herbicide on the skin or through inhalation of spray mists, anyone mixing, loading and applying Silverado WDG Herbicide must wear appropriate personal protective equipment.

Wear a long-sleeved shirt, long pants, chemical resistant gloves and shoes plus socks during mixing, loading, clean-up and repair. In addition, wear goggles or face shield during mixing/loading. Applicators must wear long-sleeved shirt, long pants and shoes plus socks.

In addition, standard label statements to protect against drift during application were added to the labels.

Environment

A hazard statement was added to the product label because of the end-use product's toxicity to non-target terrestrial plants. Buffer zones of one metre (terrestrial habitats) are required for their protection.

Next Steps

Before making a final registration decision on mesosulfuron-methyl, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications. 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

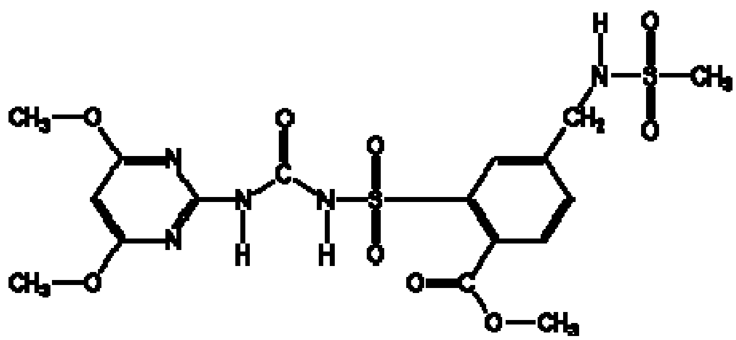
When the PMRA makes its registration decision, it will publish a Registration Decision on mesosulfuron-methyl (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application,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

Science Evaluation

Mesosulfuron-methyl

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Mesosulfuron-methyl
Function	Herbicide
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Methyl 2-[(4,6-dimethoxypyrimidin-2-ylcarbamoyl)sulfamoyl]-α-(methanesulfonamido)-*p*-toluate
2. Chemical Abstracts Service (CAS)	Methyl 2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-4-[[(methylsulfonyl)amino]methyl]benzoate
CAS number	208465-21-8
Molecular formula	$C_{17}H_{21}N_5O_9S_2$
Molecular weight	503.50
Structural formula	
Purity of the active ingredient	96.4% nominal

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

Technical Product—Mesosulfuron-methyl Technical

Property	Result
Colour and physical state	Cream-coloured powder
Odour	Weakly pungent
Melting range	189–192˚C
Boiling point or range	N/A at atmospheric pressure since it decomposes immediately after melting
Specific gravity	1.53
Vapour pressure at 20°C	3.5×10^{-12} Pa
Henry's law constant at 20°C	3.6×10^{-17} atm.m$^{3}\cdot$mol^{-1}
Ultraviolet (UV)-visible spectrum	Solvent / λ_{max} / Molar extinction coefficient (L/mol•cm) methanol / 203 / 53566 methanol/NaOH / 242 / 27918 No absorption was observed above 350 nm.
Solubility in water at 20°C	pH / medium — Solubility (g/L) 5.66 / water — 0.0214 4 / buffer — 0.00215 5 / buffer — 0.00724 7 / buffer — 0.483 9 / buffer — 15.39 10 / buffer — 13.8 (estimated by preliminary test)
Solubility in organic solvents at 20°C (g/100 mL)	Solvent — Solubility (g/L) n-hexane — <0.000229 toluene — 0.0126 isopropanol — 0.096 ethyl acetate — 2.03 dichloromethane — 3.79 acetonitrile — 8.37 acetone — 13.66
n-Octanol-water partition coefficient (K_{ow})	pH — log K_{ow} 4 — 1.90 5 — 1.39 7 — -0.48 9 — -2.06 10 — -2.10
Dissociation constant (pK_a)	4.35
Stability (temperature, metal)	Stable to metals, metal ions and elevated temperatures

End-Use Product—Silverado WDG Herbicide

Property	Result
Colour	Not required
Odour	Not required
Physical state	Solid
Formulation type	Wettable granules
Guarantee	2% nominal
Container material and description	250 g to 25 kg, plastic recyclable polyethylene
Bulk density	0.56 g/mL
pH of 10% dispersion in water	9.10
Oxidizing or reducing action	Not expected
Storage stability	Stable for one year in non-fluorinated high density polyethylene containers under warehouse conditions; however, fluorine gas barrier treatment is recommended to reduce possible solvent odour
Corrosion characteristics	Not corrosive to any packaging material tested (plain steel, stainless steel #316, aluminum, brass, copper, high-density polyethylene, Teflon, nylon, Viton, and ethylene propylene diene monomer).
Explodability	Not expected to be explosive

1.3 Directions for Use

Silverado WDG Herbicide is a selective herbicide for use as a postemergence treatment on wheat (spring and durum) for the control of wild oats. The product is to be applied at a rate of 125 g product/ha (2.5 g a.i./ha) plus the addition of Hasten Spray Adjuvant at 1.75 L/ha in a minimum water volume of 93.5 litres of water per hectare, as a broadcast treatment with ground application equipment only. Silverado WDG Herbicide may be applied once per growing season. There are no tank mix combinations with Silverado WDG Herbicide.

1.4 Mode of Action

Silverado WDG Herbicide contains the active ingredient mesosulfuron-methyl, which belongs to the sulfonylurea family of herbicides, and is classified as a Group 2 Herbicide (refer to Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*, for details). The primary mode of action of Silverado WDG is to block the enzyme acetohydroxyacid synthase. Without this enzyme weeds typically die within 4 to 6 weeks after application.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

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

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

Gas chromatography with mass spectrometry (GC-MS) and high-performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) methods were developed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media. Methods for residue analysis are summarized in Appendix I, Table 1.

Liquid chromatography with mass spectrometry (LC-MS/MS) methods were developed for data generation and enforcement purposes in plant and animal commodities. These methods fulfilled the requirements with regards to specificity, accuracy and precision at the respective limits of quantitation of the methods. Acceptable recoveries (70–120%) were obtained in plant and animal matrices. The enforcement method for plant matrices was successfully validated in wheat by an independent laboratory. Adequate extraction efficiencies were demonstrated using radiolabelled wheat analyzed with the enforcement method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for mesosulfuron-methyl was conducted. The database is complete, consisting of the full array of toxicity studies currently required for 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 high, and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product.

Technical active ingredient mesosulfuron-methyl was of low acute oral and dermal toxicity and of slight toxicity by the inhalation route in rats. It was not irritating when applied to the skin of rabbits but was minimally irritating to rabbit eyes. There was no sign of dermal reaction in the Maximization Sensitization test using guinea pigs.

The end-use-product Silverado WDG Herbicide, containing 2.26% of the technical mesosulfuron-methyl, was similar in acute toxicity to the active ingredient via the oral and dermal routes. Silverado WDG Herbicide was of low toxicity by the inhalation route. It was minimally irritating to the skin but moderately irritating to the eye of the rabbit. It was not a skin sensitizer.

The absorption, distribution, metabolism and excretion of mesosulfuron-methyl was studied in rats. Recovery of the administered dose was very high, predominantly through the feces within 24 hours (80–97% of the administered dose). Absorption was rapid but incomplete. Urinary excretion accounted for 1–4% of the administered dose except for the low dose group, which generally exhibited a slightly higher percentage in urine and slightly lower percentage of administered dose in feces compared to the high dose group. Biliary excretion accounted for 7–9% of the administered dose in the low dose group. There was no mesosulfuron-methyl in expired air and no evidence to suggest bioaccumulation. Following administration of mesosulfuron-methyl, distribution to tissues was minimal with the highest accumulation occurring in the plasma, blood and liver. Concentrations in all tissues (except residual carcass) were generally higher in males at three hours post-dosing than in females. Metabolite identification indicated that 87–97% of the administered dose was excreted unchanged as mesosulfuron-methyl. Total unidentified compounds accounted for less than 1.3% of the administered dose. The major metabolism pathway of mesosulfuron-methyl involves the breakdown of the sulfonylurea-bridge, O-demethylation, cleavage of the methanesulfonamidomethyl side chain, and hydrolysis of the methyl ester.

There were no treatment-related effects noted in short-term (90-day) studies in the mouse, rat and dog or in long-term studies in the mouse and rat up to and including the limit dose. In a 12-month dietary study in dogs, increased mucous secretion in the cardiac and fundic sections of the stomach (three males) and increased chronic superficial gastritis in the cardiac, fundic and pyloric antrum regions of stomach (one male) were noted. Effects were only observed following treatment with mesosulfuron-methyl at a very high level for an extended period (it was not observed after 90 days). There were no other effects noted at this dose level. Furthermore, there were no treatment related histological changes in females at this dose level or in either sex at lower dose levels.

No evidence of mutagenic potential of mesosulfuron-methyl was observed in a battery of in vitro and in vivo genotoxicity assays assessing gene mutation and chromosome aberration. There was no evidence of carcinogenic potential in long-term rat and mouse studies.

When tested in the rat, up to the limit dose, mesosulfuron-methyl did not affect reproductive performance, offspring viability, sexual maturation, estrous cycle or sperm parameters. Developmental studies in the rat and rabbit did not demonstrate any maternal or developmental toxicity up to the limit dose. Mesosulfuron-methyl was not teratogenic and there was no indication of increased sensitivity of the young to the test substance in any of the studies.

There was no evidence of neurotoxicity in the database.

Results of the acute and chronic tests conducted on laboratory animals with Mesosulfuron-methyl Technical and its associated end-use product, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix 1, Tables 2, 3, and 4.

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 take into account completeness of 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, rat and rabbit data were available for mesosulfuron-methyl. There was a two-generation reproductive toxicity study in rats and prenatal developmental toxicity studies in both rats and rabbits. There were no triggers to warrant a study to investigate the potential for developmental neurotoxicity.

With respect to concerns relevant to the assessment of risk to infants and children, there was no indication of increased susceptibility of rat or rabbit fetuses to in utero exposure to mesosulfuron-methyl. There was no indication of increased susceptibility in the offspring compared to parental animals up to the limit dose in the reproduction and developmental studies. No adverse effects were noted in the fetuses or pups, up to and including the limit dose.

Overall, the database is complete and there was no indication of any adverse effects to fetuses in utero or offspring. On the basis of this information, the 10-fold factor required under the *Pest Control Products Act* was reduced to 1-fold for all risk scenarios.

3.2 Determination of Acute Reference Dose

A toxicity endpoint attributable to a single dose was not identified. Therefore, the establishment of an acute reference dose was not required.

3.3 Determination of Acceptable Daily Intake

The recommended acceptable daily intake (ADI) for mesosulfuron-methyl is 1.55 mg/kg bw/day based on a no observed adverse effect level (NOAEL) of 155 mg/kg bw/day from a 12-month dietary dog toxicity study. At the lowest observed adverse effect level (LOAEL) of 574 mg/kg bw/day there was increased mucous secretion in the cardiac and fundic sections of the stomach and increased chronic superficial gastritis in the cardiac, fundic and pyloric antrum regions of the stomach. This effect was considered mild and a conservative endpoint when used for risk assessment. The applied factors included the standard 100-fold uncertainty factor to account for interspecies extrapolation and intraspecies variability. As noted in Section 3.1.1, the *Pest Control Products Act* factor was reduced to one-fold. The composite assessment factor is therefore 100.

The ADI is calculated according to the following formula:

$$ADI = \frac{155 \text{ mg/kg bw/day}}{100} = 1.55 \text{ mg/kg bw/day of mesosulfuron-methyl}$$

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

For short-term dermal and inhalation exposure, the NOAEL of 648 mg/kg bw/day in males from the 90-day dietary dog study was considered most appropriate. No treatment related effects were observed.

For intermediate to long-term dermal and inhalation exposure, the 12-month dietary dog toxicity study with a NOAEL of 155 mg/kg/day was considered most appropriate. The LOAEL of 574 mg/kg bw/day was based on increased mucus secretion in the cardiac and fundic sections of the stomach and chronic superficial gastritis. This was a localized effect as a consequence of oral treatment with mesosulfuron-methyl at a very high level for an extended period. Furthermore, there were no treatment-related histological changes in females at the high level or in either sex at lower-dose levels. It is therefore considered to be a conservative endpoint.

The target margin of exposure (MOE) for all endpoints is 100 accounting for the standard uncertainty factors of 10-fold for interspecies extrapolation and 10 fold for intraspecies variability. This is considered protective for all populations, including nursing infants and unborn children of female workers exposed to this active ingredient.

3.4.1.1 Dermal Absorption

In the absence of a dermal absorption study, a value of 100% dermal absorption was assumed.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Mixer/loader/applicator Exposure and Risk Assessment

Farmers and custom pesticide applicators may be exposed to Silverado WDG Herbicide when mixing, loading or applying this product to wheat fields. Silverado WDG Herbicide is applied at a rate of 2.5 grams of mesosulfuron-methyl per hectare. A farmer can typically treat up to 150 hectares per day using groundboom equipment and a custom applicator can typically treat up to 300 hectares per day using the same equipment. A farmer may be exposed for less than one week per year, while a custom applicator may be exposed for up to two months over the course of a year.

Exposure estimates for mixers, loaders and applicators are based on data from the Pesticide Handlers Exposure Database (PHED) Version 1.1. PHED is a compilation of generic mixer/loader/applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates. Appropriate subsets of A- and B-grade data (high confidence) were created from the database files of PHED for liquid formulation using open mixing/loading and open cab groundboom application. All data were normalized for kilograms of active ingredient handled. Exposure estimates are presented on the basis of the best-fit measure of central tendency (in other words, summing the measure of central tendency for each body part that is most appropriate to the distribution of data for that body part). Exposure estimates are based on unit exposure values from PHED, coupled with application rate and typical area treated per day inputs.

The exposure estimates are based on mixers and loaders wearing a single layer of clothing (long pants and long sleeved shirt) and gloves. Applicator exposure estimates were based on a single layer of clothing (no gloves). The estimated worker exposure was based on a worker's body weight of 70 kg and dermal absorption of 100%.

For the short-term risk assessments, MOEs were generated based on the NOAEL of 648 mg/kg bw/day from the 90-day dietary dog study. For the intermediate term risk assessments, MOEs were generated based on the NOAEL of 155 mg/kg bw/day from the 12-month dietary dog study All MOEs are above the target MOE of 100; therefore, they are considered acceptable (Table 3.4.3.1).

Table 3.4.2.1.1 Mixer, Loader and Applicator Exposure Summary

Scenario	Application rate (kg a.i./ha)	Area treated per day (ha/day)	Amount of a.i. handled per day (kg a.i./day) [1]	Combined Daily Exposure (µg a.i./kg bw/day) [2]	MOE [3]
Farmer M/L/A	0.0025	150	0.375	1.06	611,321
Custom M/L		300	0.75	1.77	87,788
Custom A				0.36	426,242

Note: Personal protective equipment – Mixer/Loaders: Long pants, long sleeves, gloves; Applicators: Long pants, long sleeves, no gloves

1 Amount of a.i. handled per day calculated using the application rate × area treated per day

2 Daily exposure was calculated using amount of a.i. handled per day × PHED unit exposure value (dermal + inhalation)/body weight (70kg). A default dermal absorption value of 100% was used.

3 Estimates of exposure for Farmers M/L and A (short term) were compared to a NOAEL of 648 mg/kg bw/day established in the 90-day oral study in dogs, target MOE = 100. Estimates of exposure for custom M/L and A (intermediate term) were compared to a NOAEL of 155 mg/kg bw/day established in the 12-month dietary study in dogs, target MOE = 100.

3.4.2.2 Exposure and Risk Assessment for Workers Entering Treated Areas

There is potential for exposure to workers re-entering areas treated with Silverado WDG Herbicide to scout or perform irrigation. Inhalation exposure is not expected to be of concern since the product is not volatile and workers are not allowed to enter treated fields for 12 hours after application. The duration of exposure is considered to be intermittent over a short period since the product is applied only once per season and residues on treated surfaces should not be available for dislodging after 30 days (short-term exposure). The primary route of exposure for workers re-entering treated areas would be through dermal contact with treated wheat.

Dermal exposure to workers entering treated areas is estimated by coupling dislodgeable foliar residue values with activity-specific transfer coefficients. Activity transfer coefficients are based on generic data from the Agricultural Re-entry Task Force (ARTF) of which Bayer CropScience is a member. Chemical-specific dislodgeable foliar residue data were not submitted. As such, a default dislodgeable foliar residue value of 20% of the application rate was used in the exposure assessment.

Exposure estimates were compared to the toxicological endpoint to obtain the MOE. The calculated MOE was well above the target MOE of 100 and therefore, not of concern.

Table 3.4.2.2.1 Postapplication Margin of Exposure on Wheat

	Transfer Coefficient (cm^2/hr) A	DFR Value (μg/cm^2) B	Time (hr/day)	Exposure Estimate (mg/kg bw/day) C	MOE D
Scouting/ Irrigation	1500	0.005	8	0.0009	720,000

A Transfer coefficients are based on Agricultural Re-entry Task Force data. The applicant, Bayer CropScience Inc., is a member of Task Force. Transfer coefficient values are as documented in United States Environmental Protection Agency's Science Advisory Council for Exposure. Policy Number 003.1. May 7.

B A chemical specific dislodgeable foliar residue (DFR) study was not submitted. A default value of 20% of the application rate was chosen during the day of application to estimate exposure from foliar contact.

C Exposure estimates were calculated using the following formula:

$$\frac{\text{DFR Value } (\mu g/cm^2) \times \text{Transfer Coefficient } (cm^2/hr) \times \text{Hours Worked per Day (hr)} \times \text{Conversion Factor } (1mg/1000\mu g)}{\text{Body Weight (70 kg)}}$$

D MOEs calculated using a NOAEL of 648 mg/kg bw/day from the 90-day oral study in dogs.

3.4.2.3 Bystander Exposure and Risk

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

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products and animal commodities is mesosulfuron-methyl. The LC-MS/MS enforcement analytical method is valid for the quantification of mesosulfuron-methyl residues in wheat, and the LC-MS/MS data-gathering analytical method is valid for determination of residues in livestock matrices. The residues of mesosulfuron-methyl are stable when stored in a freezer at -18°C for 24 months in wheat grain and for 40 months in wheat forage and straw. Mesosulfuron-methyl residues concentrated in the processed commodities wheat bran (1.3x), shorts (1.2x), germ (4.3x) and aspirated grain fractions (21.6x). Quantifiable residues are not expected to occur in livestock matrices with the current use pattern. Supervised residue trials conducted throughout the United States using end-use products containing mesosulfuron-methyl at exaggerated rates in or on wheat are sufficient to support the MRLs.

3.5.2 Dietary Risk Assessment

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

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the basic chronic analysis: 100% crop treated, experimental processing factors, residues of mesosulfuron-methyl in animal commodities based on limit of quantitation values and in crops at MRL values. The basic chronic dietary exposure from all supported mesosulfuron-methyl food uses (alone) for the total population, including infants and children, and all representative population subgroups is less than 1% of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to mesosulfuron-methyl from food and water is less than 1% (0.00016 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1–2 years old at less than 1% (0.00057 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. An acute dietary exposure analysis was not required.

3.5.3 Aggregate Exposure and Risk

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

3.5.4 Maximum Residue Limits

Table 3.5.4.1 Maximum Residue Limits

MRLs (ppm)	Foods
0.03	Wheat grain
0.10	Wheat germ
0.01	Fat, meat and meat byproducts of cattle, goats, hogs, horses and sheep; milk and eggs

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

The nature of the residues in animal and plant matrices, analytical methodologies, field trial data, and the chronic dietary risk estimates are summarized in Appendix I, Tables 1, 4 and 5.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Mesosulfuron-methyl transforms in soils and is non-persistent to moderately persistent in the terrestrial environment (laboratory DT_{50} (dissipation time to 50%): 8.56–74.8 days and field DT_{50}: 13.6 days). Hydrolysis is a major route of dissipation at acidic pH (DT_{50}: 3.5 days at pH 4) and produces two major transformation products, F092944 and F140584. Mesosulfuron-methyl is stable to hydrolysis under neutral and alkaline conditions. Phototransformation is not a major route of transformation in the terrestrial environment. Biotransformation is an important route of dissipation in soils. Laboratory biotransformation studies indicated that mesosulfuron-methyl transforms under aerobic conditions (DT_{50}: 8.56–74.8 days) and forms three major transformation products, F092944, F099095 and F154851. Under anaerobic soil conditions, mesosulfuron-methyl transforms (DT_{50}: 26.8 days) and forms one major biotransformation product, F160459.

Mesosulfuron-methyl is non-persistent to moderately persistent in aquatic systems (laboratory) under anaerobic (DT_{50}: 6.74 days) and aerobic (DT_{50}: 24.8–77.3 days) conditions. Three major transformation products are formed: F160459 (aerobic and anaerobic), F147447 (aerobic) and F160460 (anaerobic). Mesosulfuron-methyl is unlikely to accumulate in sediments.

Mesosulfuron-methyl exhibited a high to very high mobility in soils (K_{oc} = 24–298 mL/g), based on the results of laboratory soil adsorption studies. The mobility of the major soil transformation products, F154851 and F099095, is similar to the parent compound. Mesosulfuron-methyl is classified as a non-leacher to leacher according to gauss unit scores (1.42–4.9). However, mesosulfuron-methyl was not detected below 30 cm in a terrestrial field dissipation study conducted in an ecoregion relevant to the region of Canadian prairies where this product will be used). Leaching into groundwater of mesosulfuron-methyl is therefore expected to be minimal under Canadian wheat growing conditions. This has been supported by the results of groundwater modelling scenarios.

Identification of the transformation products relevant to the environment are summarized in Appendix I, Table 7.1-1. Data on the environmental fate and behaviour of mesosulfuron-methyl and its transformation products are summarized in Appendix I, Table 7.1-2.

4.2 Effects on Non-Target Species

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

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

4.2.1 Effects on Terrestrial Organisms

Risk to terrestrial organisms was based upon the evaluation of mesosulfuron-methyl toxicity data for the following (Appendix I, Table 7.2-1):

- one earthworm species (acute exposure), one species of honeybee (oral and contact exposure) representing invertebrates
- two bird and one mammal species representing vertebrates (acute, short-term, or long-term exposure)
- ten crop species representing non-target vascular plants

The uncertainty factors used in modifying the toxicity values are summarized in Appendix I, Table 7.2-2.

For assessment of earthworms, a screening level EEC in soil of 0.0011 mg mesosulfuron-methyl/kg dry soil was used. This is based on the initial EEC on soil immediately following application based on a soil density of 1.5 g/cm^3, soil depth of 15 cm, and the rate of 2.5 g mesosulfuron-methyl/ha. The toxicity endpoint used for assessment of acute effects of mesosulfuron-methyl was LC_{50} (lethal concentration to 50%) >1000 mg/kg dry soil. The screening level RQ value was <0.01 (Appendix I, Table 7.2-3a). Therefore, negligible risk to earthworms is expected.

For assessment of bees, a screening level EEC for acute oral or contact exposure to residues is 2.5 g mesosulfuron-methyl/ha. For bees, the LD_{50} (lethal dose to 50%) values in µg/bee were converted to the equivalent rates in kg/ha. The converted LD_{50} value was >14.56 kg mesosulfuron-methyl/ha. The screening level RQ value was <0.01 (Appendix I, Table 7.2-3a). Therefore, negligible risk to honeybees is expected.

For the assessment of birds and small wild mammals, the EEC values for mesosulfuron-methyl in potential food items were determined for a direct application immediately after a spray of 2.5 g mesosulfuron-methyl/ha. The screening level estimated daily exposure values were dependent on the body weight of an organism (20, 100, 1000 g for birds and 15, 35, 1000 g for mammals), food preferences (100% small insects for insectivores, 100% fruits for frugivores, 100% grain and seeds for granivores, and 100% leaves and leafy crops for herbivores), and amount consumed on a daily basis. The mesosulfuron-methyl toxicity endpoints used were LD_{50} >2000 and >5000 mg/kg bw for acute assessment of birds and small mammals, respectively; LD_{50} >720 mg/kg bw/day for short-term dietary assessment of birds; no observed effect level (NOEL) 908 mg/kg bw/day for short-term dietary assessment of small mammals; NOEL 93 mg/kg bw/day for long-term assessment of birds based on reproductive performance and NOEL 1175 mg/kg bw/day for long-term assessment of small wild mammals based reproductive performance. All screening level RQ values were <0.01 for birds and small wild mammals (Appendix I, Table 7.2-3b). Therefore, negligible risk to birds and small wild mammals is expected.

For assessment of non-target plants, a screening level EEC is based on direct exposure to the 2.5 g mesosulfuron-methyl/ha application. To assess the impact of mesosulfuron-methyl, the toxicity endpoint used was the 5th percentile hazard rate (HR_5 = 0.34 g a.i./ha) based on the species sensitivity distribution of the EC_{50} data for the most sensitive endpoint. In this case, the most sensitive endpoint for the majority of the plant species is dry weight (biomass). The screening level RQ value was 7.15 (Appendix I, Table 7.2-3a). An RQ for drift deposition at one metre downwind (6% of applied) from the point of application indicates that impacts on non target terrestrial plants adjacent to the treatment area are not of concern ($RQ = 2.5 \times 0.06 \div 0.349 = 0.4$). Thus, to mitigate potential risk from spray drift, a one meter default buffer zone is required for terrestrial habitats.

4.2.2 Effects on Aquatic Organisms

Risk of mesosulfuron-methyl to aquatic organisms was based upon the evaluation of mesosulfuron-methyl toxicity data for the following (Appendix I, Table 7.2-1):

- one freshwater and one marine invertebrate shrimp species and one bivalve species (acute or chronic exposure)
- two freshwater and one marine fish species (acute exposure)
- two freshwater and one marine algal species, and one vascular plant species

The uncertainty factors used in modifying the toxicity values are summarized in Appendix I, Table 7.2-2.

Screening level EEC values for mesosulfuron-methyl in water were calculated assuming a reasonable conservative scenario of direct application to water bodies of two different depths (80 cm and 15 cm). The 80-cm deep water body is chosen to represent a permanent body of water and 15 cm deep is chosen to represent a seasonal body of water. The pesticide is assumed to be instantaneously and completely mixed within the water body.

For assessment of fish, aquatic invertebrates, algae, and aquatic vascular plants, a screening level EEC of mesosulfuron-methyl in a permanent water body (80-cm water depth) is 0.0003125 mg/L based on an application rate of 2.5 g mesosulfuron-methyl/ha. The transformation products are also screened at this concentration assuming 100% conversion from parent adjusting for the molar ratio. The EEC of transformation products in permanent water body are 0.00018 mg for F147447/L, 0.00030375 mg for F160459/L and 0.000295 mg for F160460/L.

The toxicity endpoints used for assessment of acute effects were LC_{50} >91.5 mg/L for acute exposure of fish; EC_{50} >90.2 mg/L for acute exposure of invertebrate (crustaceans and molluscs) to mesosulfuron-methyl. The toxicity endpoints used for assessment of long-term effects were no observed effect level (NOEC) 1.7 mg/L for chronic exposure of invertebrates to technical mesosulfuron-methyl based on terminal dry weight. For algae, the toxicity endpoints used were EC_{50}: 0.21 mg/L for technical mesosulfuron-methyl; EC_{50}: 98.4 mg/L for transformation product F160459 and EC_{50} >92.0 mg/L for transformation product F147447 based on biomass. For aquatic vascular plants, the toxicity endpoints were EC_{50}: 0.00064 mg/L for technical mesosulfuron-methyl, EC_{50} >94.71, 1.5, and >90.33 mg/L for transformation products F160460, F160459 and F147447, respectively, based on frond number or biomass.

All screening level RQ values were <1 (Appendix I, Table 7.2-3c). Therefore, there are no concerns about the use of mesosulfuron-methyl affecting fish, aquatic invertebrates, algae and plants.

For assessment of amphibians, a screening level EEC of mesosulfuron-methyl in a seasonal water body (15-cm water depth) is 0.0016mg/L based on an application rate of 2.5 g mesosulfuron-methyl/ha. Based on fish toxicity data, RQ values were <0.01 for acute exposure (Appendix I, Table 7.2-3c). Therefore, there are no concerns about the use of mesosulfuron-methyl affecting amphibians.

5.0 Value

5.1 Effectiveness Against Pests

Efficacy data were submitted from 29 replicated efficacy field trials conducted over a four-year period (2002–2005) at several locations in four northern American states (North Dakota, Minnesota, Montana and South Dakota). All trials were conducted in wheat crops where Silverado WDG Herbicide was applied at 75 and 125 g product/ha (1.5 and 2.5 g a.i./ha) in the field trials designed to assess the efficacy at various rates. The herbicide treatments were applied using small plot application equipment. The efficacy of Silverado WDG Herbicide was visually assessed as percent weed control of wild oats and compared to an untreated weedy check. Observations were made up to two times throughout the growing season.

5.1.1 Acceptable Efficacy Claims

The submitted efficacy data support the weed control claim of Silverado WDG herbicide applied alone at 125 g/ha (2.5 g a.i./ha) plus Hasten (methylated seed oil) Spray Adjuvant at 1.75 L/ha using one postemergence application per season applied by ground equipment to control wild oats in spring and durum wheat.

5.2 Phytotoxicity to Host Plants

Data from 40 trials conducted in five northern American states during a five-year period (2001–2005) were submitted in support of crop tolerance claims for spring and durum wheat. Spring wheat was planted in 31 trials conducted over three years, distributed in North Dakota, Minnesota, Montana, South Dakota and Idaho. Durum wheat was planted in 10 trials conducted during a five-year period, distributed in North Dakota and Minnesota. Silverado WDG Herbicide was applied at 125 and 250 g product/ha (2.5 and 5.0 g a.i./ha) in the field trials designed to assess crop tolerance at the 1x and 2x rates.

Crop injury (%) was visually assessed up to three times during the growing season. Crop yield, expressed as a percentage of an untreated check, was reported in four out of 31 spring wheat trials and two out of 10 durum wheat trials.

5.2.1 Acceptable Claims for Host Plants

Crop injury to spring and durum wheat treated with Silverado WDG Herbicide applied alone was less than 10% at the late season rating. Crop yield was also comparable to registered commercial treatments.

5.3 Impact on Succeeding Crops

The impact of mesosulfuron-methyl on succeeding crops was addressed in the application for Silverado WDG Herbicide. Data from a total of 15 trials were submitted for review conducted in spring wheat, durum wheat, spring barley, sunflowers, soybean, lentils, dry beans, field peas, sugarbeets, potatoes, canola, and field corn.

5.3.1 Acceptable Claims for Succeeding Crops

Based on the evidence made available, claims for spring wheat, durum wheat, spring barley, sunflowers, soybeans, lentils, dry beans, field peas, sugarbeets, potatoes, and canola with a 10 month re-cropping interval and field corn with a 12 month re-cropping interval can be supported from a crop tolerance perspective.

5.4 Economics

Wheat is Canada's most important field crop, individually out-producing all other cereal, pulse, oilseed and hay crops. In 2006, wheat was grown on nearly 10.6 million hectares and produced about 27.3 million tonnes of grain. The majority of spring and durum wheat is grown in Western Canada. In 2006, Saskatchewan, Manitoba and Alberta produced 98% and 100% of Canada's spring wheat and durum wheat, respectively. Wheat is also Canada's largest Agri-food export. In 2003 and 2004, Canada exported $2.826 and $3.479 billion (CDN), respectively. These wheat exports accounted for 11% and 13% of the total Canadian agri-food exports, respectively.

Wild oat is the most serious grassy weed in the Canadian Prairies. Losses due to this weed can be as high as $500 million annually across the Prairie provinces. It causes yield losses, dockage losses, cleaning costs, and lowers grade and quality. Yield loss depends on the number of wild oats per square metre and the stage of the wild oats and the crop. Wild oat is very competitive with wheat. Left unchecked, 10 wild oat plants per square metre can reduce wheat yields by 10%.

5.5 Sustainability

5.5.1 Survey of Alternatives

Several non-chemical methods of control are available to growers. These include use of a diverse crop rotation, ensuring that fence lines, ditches and wastelands are kept weed-free, keeping equipment clean, ensuring adequate composting of all animal wastes spread on fields, maintaining good soil fertility, mechanically controlling emerged weeds, the use of certified seed, use of increased crop seeding rates and/or reduced row spacing, appropriate seeding time, use of biological control agents, etc.

Silverado WDG represents an additional option for wild oat control utilizing a group 2 herbicide mode of action in spring and durum wheat. Within herbicide group 2, Silverado WDG offers western Canadian growers additional choice with a reduced rate of required active ingredient and limited rotational cropping issues as identified on the label.

The key herbicide options currently available for postemergence control of wild oats in spring and/or durum wheat are summarized in Table 9 of Appendix I. These alternatives fall into three categories:

- Group 1 herbicides that control annual grasses only
- Combination products that contain three active ingredients, belonging to at least two mode of action groups
- Group 2 herbicides that control wild oats and some broadleaf weeds

5.5.2 Compatibility with Current Management Practices Including Integrated Pest Management

Mesosulfuron-methyl, the active ingredient of Silverado WDG, provides an additional choice within herbicide group 2 for herbicide group rotation when controlling wild oat. The use of Silverado WDG does not restrict the sequential use of other chemicals of alternate modes of action. Refer to the label for information on the rotational cropping profile of Silverado WDG Herbicide.

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

For resistance management, mesosulfuron-methyl is considered a member of the sulfonylurea chemical family within the acetolactate synthase/acetohydroxy acid synthase inhibitor mode of action, commonly referred to as Group 2. Any weed population may contain or develop plants naturally resistant to mesosulfuron and other Group 2 herbicides.

Silverado WDG provides selected wild oat control with its single mode of action. Due to the low application rate of Silverado WDG and it’s limited persistence relative to earlier Group 2 herbicides, Silverado WDG could be selected as the Group 2 product used within a herbicide rotation designed to manage or avoid the development of herbicide resistance or to be used as a rescue treatment in the situation of product failure due to Group 1 resistance.

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

5.5.4 Contribution to Risk Reduction and Sustainability

The low application rate of Silverado WDG reduces environmental and user exposure to the active ingredient. The crop rotation profile of Silverado WDG allows producers the freedom to maintain a diverse crop rotation, a management practice that is recommended to reduce pest pressures and delay the onset of herbicide resistance. These factors act in combination to reduce the risk to the environment and to the producer.

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: 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, Mesosulfuron-methyl and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Mesosulfuron-methyl does not meet Track 1 criteria, and is not considered a Track 1 substance. See Table 10 for comparison with Track 1 criteria.
- Mesosulfuron-methyl does not form any transformation products that meet all Track 1 criteria.

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*.[3] The

[3] *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*

list is used as described in the PMRA Notice of Intent NOI2005-01[4] and is based on existing policies and regulations including Regulatory Directives DIR99-03 and DIR2006-02, *Formulants Policy and Implementation Guidance Document*, 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 Mesosulfuron-methyl and the end-use product Silverado WPG Herbicide do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*
- The end-use product Silverado WPG Herbicide does not contain any formulants of health or environmental concern identified in the *Canada Gazette*. However, the end-use product does contain an aromatic petroleum distillate. Therefore, the label for the end-use product Silverado WPG Herbicide will include the statement: “This product contains aromatic petroleum distillates that are toxic to aquatic organisms.”

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

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for mesosulfuron-methyl is adequate to define the majority of toxic effects that may result from exposure to mesosulfuron-methyl. In subchronic and chronic studies on laboratory animals, there was no significant indication of toxicity and no primary target organs identified. However, increased mucous secretion in the cardiac and fundic sections of the stomach and chronic superficial gastritis were noted in the 12-month dietary toxicity study in dogs. This finding was considered mild. There was no evidence of carcinogenicity in rats or mice after longer-term dosing. There was no evidence of increased susceptibility of the young in reproduction or developmental toxicity studies. Mesosulfuron-methyl is not considered to be a neurotoxicant. In general mesosulfuron-methyl exhibited low toxicity in all species tested.

The nature of the residue in plants (wheat) and animals (hen and cow) is adequately understood. The residue definition for enforcement purposes in plant products and animal matrices is mesosulfuron-methyl. The use of mesosulfuron-methyl on wheat does not constitute an unacceptable chronic dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend MRLs to protect human health. The PMRA recommends that the following MRLs be specified for residues of mesosulfuron-methyl in and on wheat.

Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.

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

MRLs (ppm)	Foods
0.03	Wheat grain
0.10	Wheat germ
0.01	Fat, meat and meat byproducts of cattle, goats, hogs, horses and sheep; milk and eggs

7.2 Environmental Risk

There are no concerns about the use of mesosulfuron-methyl affecting earthworms, bees, birds, mammals, fish, aquatic vascular plants, aquatic invertebrates, plants and algae. Risk of adverse effects to terrestrial plants was identified from an initial screening level assessment. A refined assessment looking at drift deposition at one metre downwind from the point of application indicates there is no concern about negative impacts on non-target terrestrial plants adjacent to the treatment area. Therefore, a default buffer zone of one metre is required for sensitive terrestrial habitats.

7.3 Value

The data submitted to register Silverado WDG Herbicide are adequate to support its use in wheat (spring and durum). Silverado WDG Herbicide provides control of wild oats a problematic weed in western agriculture, with a single application to wheat (spring and durum). Crop tolerance and yield response to the application of Silverado WDG Herbicide is also acceptable. Silverado WDG Herbicide (Group 2) provides an alternative mode of action to commonly used Group 1 herbicides.

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 Mesosulfuron-methyl Technical Herbicide and Silverado WDG Herbicide containing the technical grade active ingredient Mesosulfuron-methyl, used to control wild oats in spring and durum wheat.

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

μg	microgram
a.i.	active ingredient
AD	administered dose
ADI	acceptable daily intake
atm	atmosphere
bw	body weight
DT_{50}	dissipation time 50% (the time required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the time required to observe a 90% decline in concentration)
EC_{25}	effective concentration on 25% of the population
EDE	estimated daily exposure
EEC	expected environmental concentration
g	gram
GC	gas chromatography.
ha	hectare(s)
HAFT	highest average field trial
HPLC	high performance liquid chromatography
K_d	soil-water partition coefficient
kg	kilogram
K_{oc}	organic-carbon partition coefficient
K_{ow}	octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOQ	limit of quantitation
LR_{50}	lethal rate 50%
LSC	liquid scintillation counting
mg	milligram
mL	millilitre
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NAFTA	North American Free Trade Agreement
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NR	not reported
PBI	plantback interval
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
ppm	parts per million

RQ	risk quotient
STMR	supervised trial mean residue
STMR	supervised trial median residue
TLC	thin layer chromatography
TP	transformation product
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ		Reference
Plant	EM F08/99-0 Enforcement method	Mesosulfuron-methyl	LC-MS/MS (liquid chromatography with mass spectrometry)	0.01 ppm 0.05 ppm	Wheat grain Wheat straw and forage	1437158
	RAM CK/03/00	Mesosulfuron-methyl	LC-MS/MS	0.01 ppm 0.05 ppm	Wheat and barley grain Wheat straw, hay and forage; and barley straw and hay	1437157
	DGM F02/99-0	Mesosulfuron-methyl	LC-MS/MS	0.01 ppm 0.05 ppm	Wheat grain Wheat straw and forage	1437155
Animal	EM F07/00-0 Enforcement method	Mesosulfuron-methyl	LC-MS/MS	0.01 ppm	Meat, fat, liver, kidney, eggs, milk	1634543
Soil	None provided	parent	HPLC-MS/MS	0.01 mg/kg		1633685 and 1758286
	None provided	AE F099095	HPLC-MS/MS	0.01 mg/kg		1633685 and 1758286
	None provided	AE F154851	HPLC-MS/MS	0.01 mg/kg		1633685 and 1758286
	None provided	AE F092044	GC-MS	2 µg/kg		1633684 and 1758286
Sediment	None provided	parent and transformation products	Extended from soil			1453429
Water	None provided	parent	HPLC-MS/MS	0.05 µg/L		1758287 and 1798481
	None provided	AE F160459	HPLC-MS/MS	0.05 µg/L		1758287 and 1798481
	None provided	AE F147447	HPLC-MS/MS	0.03 µg/L		1758287 and 1798481

Table 2 Acute Toxicity of Mesosulfuron-methyl and Its Associated End-use Product Silverado WDG Herbicide

Study Type	Species	Result	Comment	Reference PMRA#
Acute Toxicity of Mesosulfuron-methyl (Technical)				
Oral	Rats	LD_{50} >5000 mg/kg bw	Low Toxicity	1436958
Dermal	Rats	LD_{50} >5000 mg/kg bw	Low Toxicity	1436959
Inhalation	Rats	LC_{50} >1.33 mg/L	Slight Toxicity	1436960
Skin irritation	Rabbits	MAS = 0	Non-Irritating	1436962
Eye irritation	Rabbits	MAS = 0.67/110, MIS = 12.7/110 (1hr)	Minimally Irritating	1436961
Skin sensitization	Guinea pigs	No dermal reaction noted	Not a dermal sensitizer	1436963
Acute Toxicity of End-Use Product – Silverado WDG Herbicide				
Oral	Rats	LD_{50} >2000 mg/kg bw	Low Toxicity	1453521
Dermal	Rats	LD_{50} >2000 mg/kg bw	Low Toxicity	1453522
Inhalation	Rats	LC_{50} >2.44 mg/L	Low Toxicity	1453523
Skin irritation	Rabbits	MAS = 0.33/8.0	Minimally Irritating	1453525
Eye irritation	Rabbits	MAS = 34.45/110, MIS = 49.36/110 (24hr)	Moderately Irritation	1453524
Skin sensitization	Guinea pigs	No dermal reaction noted	Not a dermal sensitizer	1453526

a MAS = maximum average score for 24, 48 and 72 hours

b MIS = maximum irritation score

Table 3 Toxicity Profile of Technical Mesosulfuron-methyl

Study Type	Species	Results[a] (mg/kg/day in M/F)	Reference (PMRA #)
21-day dermal irritation	NA	A waiver rationale was submitted for this study. The acute toxicity studies indicated that mesosulfuron-methyl is of low toxicity, non-irritating to the skin and minimally irritating to the eyes. No significant effects were observed in oral short-term studies. Based on the weight of evidence, the waiver rationale was considered to be acceptable.	1453395
90-day dietary	Mouse	NOAEL = 1238.3/1603.4 mg/kg bw/day M/F LOAEL not established	1501633
Carcinogenicity (18-month dietary)	Mouse	NOAEL = 1069.44/1355.60 mg/kg bw/day M/F LOAEL not established **No evidence of carcinogenicity**	1501636
90-day dietary	Rat	NOAEL = 908/1977 mg/kg bw/day M/F LOAEL not established	1456967
Chronic/ Carcinogenicity (2-year dietary)	Rat	NOAEL = 764/952 mg/kgbw/day LOAEL not established **No evidence of carcinogenicity**	1453400
90-day dietary	Dog	NOAEL = 648/734 mg/kg bw/day M/F LOAEL not established	1501635

Study Type	Species	Results[a] (mg/kg/day in M/F)	Reference (PMRA #)
1-year dietary	Dog	NOAEL = 155/646 mg/kgbw/day M/F LOAEL = 574 mg/kg bw/day Increased mucous secretion in cardiac and fundic sections of stomach (3 males) and increased superficial gastritis in the cardiac and pyloric antrum region of the stomach (1 male)	1436969
Multi-generation	Rat	**Parental toxicity**: NOAEL = 1175/1388 mg/kg bw/day M/F LOAEL not established **Offspring toxicity:** NOAEL = 1175/1388 mg/kg bw/day M/F LOAEL not established **Reproductive toxicity:** NOAEL = 1175/1388 mg/kg bw/day M/F LOAEL not established	1453402
Developmental toxicity	Rat	**Maternal:** NOAEL = 1000 mg/kg bw/day LOAEL not established **Developmental:** NOAEL = 1000 mg/kg bw/day LOAEL not established	1453403
Developmental toxicity	Rabbit	**Maternal:** NOAEL = 1000 mg/kg bw/day LOAEL not established **Developmental:** NOAEL: = 1000 mg/kg bw/day LOAEL not established	1453405
Reverse gene mutation assay	Bacteria	Negative	1453405
Gene mutations in mammalian cells in vitro	Chinese hamster	Negative	1453406/1501641
In vitro unscheduled DNA synthesis	Rat hepatocytes	Negative	1453408
In vitro mammalian chromosomal aberration	Chinese hamster	Negative	1453406/1501642
In vivo mammalian cytogenetics	Mice	Negative	1453409

Study Type	Species	Results[a] (mg/kg/day in M/F)	Reference (PMRA #)
Metabolism		**Absorption:** Rapid, but incomplete **Distribution:** No bioaccumulation observed. Radioactivity in tissues less than 0.1% At study termination radioactivity was highest in plasma, blood and liver, and was generally higher in males than females. **Excretion:** Predominantly in feces within 24 hours (80–97%) Urinary excretion accounted for 1–4% (except 13–14% in 10 mg/kg group, The biliary component accounted for 7–9% dose in this low dose group. 12 hours post dose. **Metabolism:** Limited, 6 metabolites identified Unidentified compounds were less than 1.3% dose AEF140584 was the primary metabolite, accounting for 2–5%, except in the 1000 mg/kg group of females, where it went up to 14% dose. Metabolites AEF160459, AEF147447, AEF154851, AEF151015 and AE21941 were found <1.5% of dose Main metabolic pathway involved a break down of the sulfonylurea-bridge, O-demethylation at the pyrimidine and a C1 hydroxylation of the amidomethyl carbon by cytochrome P450 monoxygenases	1453410 to 1453418

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Mesosulfuron-methyl

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	UF/SF[1] or Target MOE[2]
Acute dietary, females aged 13+	Acute reference dose = An appropriate toxicity endpoint attributable to a single dose was not identified. Therefore, an acute reference dose was not established			
Chronic Dietary	NOAEL = 155	12 month dietary dog study	Increased mucous secretion in the stomach and chronic gastritis.	100
	ADI = 1.55 mg/kg/day			
Short-term Dermal and Inhalation	NOAEL = 648 mg/kg/day in male dogs	90-day dietary dog study	LOAEL = Not established	100
Intermediate-to long term Dermal and Inhalation	NOAEL = 155 mg/kg/day	12 month dietary dog study	LOAEL = 574 mg/kg bw/day	100

[1] Dietary scenerios
[2] Exposure scenerios

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN WHEAT		PMRA #1453424 and 1453423
Radiolabel Position	**[2-^{14}C-pyrimidyl]**	**[U-^{14}C-phenyl]**
Test Site	Outdoor vegetation hall in Germany.	
Treatment	By spray at advanced tillering stage (BBCH25-29) with plant height of 20 cm.	By spray at tillering stage (BBCH23) with plant height of 25 cm.
Rate	10 or 20 g a.i./ha The higher rate treatment was made as two applications one day apart.	30 or 60 g a.i./ha The higher rate treatment was made as two applications one day apart.
End-use product	WDG formulation applied with safener at a ratio of 1:3 (a.i.: safener)	
Preharvest interval	Leaves were collected on day 0 after the spray mix dried; forage was collected at PHI of 35/36 days, hay at PHI of 49 days and mature grain and straw at PHI of 95 days.	Leaves were collected on day 0 after the spray mix dried; forage was collected at PHI of 41/42 days, hay at PHI of 57/58 days and mature grain and straw at PHI of 103/104 days.

Purified extracts and hydrolysates were radioassayed by liquid scintillation counting (LSC). Nonextractable residues were radioassayed by combustion/LSC. Total radioactive residues (TRRs) were determined by summing the radioactivity in extractable and nonextractable residues. With the pyrimidyl label, the TRRs were 0.936–1.509 ppm in leaves, 0.007 ppm in forage and 0.017 ppm in straw treated at the lower rate (10 g a.i./ha), and were 2.718 ppm in leaves, 0.019 ppm in forage, 0.011 ppm in hay, 0.019 ppm in straw and 0.001 ppm in grain treated at the higher rate (20 g a.i./ha). With the phenyl label, the TRRs were 4.048 and 9.936 ppm in leaves, 0.020 and 0.019 ppm in forage, 0.008 and 0.013 ppm in hay, 0.032 and 0.046 ppm in straw, and 0.001 and 0.001 ppm in grain treated at the 30 and 60 g a.i./ha rates, respectively.

Residues were extracted with acetonitrile/water (4:1, v/v). Solvent extractability was in the range of 67–91% in forage, hay and straw samples. In grain, 22–30% of the TRRs were extractable, with a further 58–59% of the TRRs released by cellulase/macerozyme and/or acid hydrolysis.

Since TRRs in wheat grain were too low to be identified (<0.001 ppm), characterization was carried out in straw, hay and forage samples in lieu of grain, by high-performance liquid chromatography (HPLC) and/or thin layer chromatography (TLC), and metabolites were identified by comparison of retention times with those of known standards. Mesosulfuron-methyl was identified at 2–3% of the TRRs (0.0003–0.0014 ppm) in straw, 15% of the TRRs (0.0017 ppm) in hay and 23% of the TRRs (0.0043–0.0044 ppm) in forage. The metabolite AE F160459 was identified at 4–9% of the TRRs (0.0006–0.0016 ppm). The following metabolites were additionally identified in straw and forage: AE F140584 (9–10% of the TRRs; 0.0019–0.0040 ppm), AE F160459 (13–14% of the TRRs; 0.0026–0.0058 ppm), and AE F147447 (5–18% of the TRRs; 0.0009–0.0083 ppm). The remaining extractable residues were characterized as polar residues consisting of 5–8 components and unresolved peak fractions, none of which exceeded a residue level of 0.004 ppm.

The residue definition in cereals is mesosulfuron-methyl.

Metabolites Identified	Major Metabolites (>10% TRR)		Minor Metabolites (<10% TRR)	
Radiolabel Position	**[2-^{14}C-pyrimidyl]**	**[U-^{14}C-phenyl]**	**[2-^{14}C-pyrimidyl]**	**[U-^{14}C-phenyl]**
Wheat forage	Mesosulfuron-methyl	Mesosulfuron-methyl, AE F160459, AE F140584	AE F160459	AE F147447
Wheat hay	Mesosulfuron-methyl	Not analyzed	AE F160459	Not analyzed
Wheat straw	None	AE F160459, AE F147447	Mesosulfuron-methyl, AE F160459	Mesosulfuron-methyl, AE F140584

<table>
<tr><th colspan="3">CONFINED ACCUMULATION IN ROTATIONAL CROPS – CARROT, SPINACH, WHEAT</th><th colspan="3">PMRA #1437170, 1437171, 1437172, 1437173, 1437174 and 1437175</th></tr>
<tr><td colspan="2">Radiolabel Position</td><td colspan="2">[2-^{14}C-pyrimidyl]</td><td colspan="2">[U-^{14}C-phenyl]</td></tr>
<tr><td colspan="2">Test site</td><td colspan="4">Outdoor vegetation hall</td></tr>
<tr><td colspan="2">Formulation used for trial</td><td colspan="4">WDG formulation applied to soil using pipette. Treated soil was transferred to plant containers as an even 5 cm top layer.</td></tr>
<tr><td colspan="2">Application rate and timing</td><td colspan="4">15 g a.i./ha, 31/32 days prior to planting.</td></tr>
<tr><td colspan="2">Metabolites Identified</td><td colspan="2">Major Metabolites (>10% TRR)</td><td colspan="2">Minor Metabolites (<10% TRR)</td></tr>
<tr><td>Matrix</td><td>Plantback Interval (days)</td><td>[2-^{14}C-pyrimidyl]</td><td>[U-^{14}C-phenyl]</td><td>[2-^{14}C-pyrimidyl]</td><td><b>[U-^{14}C-phenyl]</td></tr>
<tr><td>Wheat straw</td><td>31/32</td><td>Very polar unknown</td><td>AE F147447, very polar unknown</td><td>mesosulfuron-methyl, AE F092944</td><td>mesosulfuron-methyl, AE F140584, AE F154851</td></tr>
<tr><td colspan="6">TRRs were all below 0.010 ppm in/on all harvested rotational crop matrices except in wheat straw. TRRs were 0.0219, 0.0125, and 0.0144 ppm in pyrimidyl-labeled wheat straw from the 31/32, 124/125, and 368/369 plantback intervals (PBIs), respectively. TRRs were 0.0110, 0.0112, and 0.0088 ppm in phenyl-labeled wheat straw from 31/32, 124/125, and 368/369 PBIs, respectively.

The wheat straw samples from the 31/32-day rotation were subjected to further analytical work to determine the nature of the residue. Solvent extraction released about 66% and 87% of the TRRs from pyrimidyl- and phenyl-labeled wheat straw, respectively. Nonextractable residues were 10–26% of the TRRs (0.001–0.006 ppm). Residues in the organosoluble extracts of wheat straw were analyzed by HPLC. Mesosulfuron-methyl was identified in both the pyrimidyl- and phenyl-labeled wheat straw at 2.0–3.5% of the TRRs (0.0004 ppm). The AE F147447 metabolite was the predominant residue (30.8% TRR, 0.0034 ppm) in phenyl-labeled wheat straw. AE F140584 and AE F154851 were additionally identified as minor metabolites each at ≤6% of the TRRs (0.0003–0.0006 ppm) in phenyl-labeled wheat straw. The AE F092944 metabolite was identified as a minor residue (7.2% TRR, 0.0016 ppm) in pyrimidyl-labeled wheat straw, in addition, up to 7 unknowns were characterized in wheat straw with each unknown detected at <8% of the TRRs (≤0.0012 ppm), except for one very polar unknown in the pyrimidyl-labeled straw which was present at 33.6% of the TRRs (0.0074 ppm) and one very polar unknown in the phenyl-labeled straw which was present at 13.1% of the TRRs (0.0014 ppm).

The metabolic pathway of mesosulfuron-methyl in rotational crops proceeds via similar processes as in the primary crop wheat.

The residue definition in rotational crops is mesosulfuron-methyl.</td></tr>
</table>

CONFINED ACCUMULATION IN ROTATIONAL CROPS – CARROT, SPINACH, WHEAT	PMRA #1437170, 1437171, 1437172, 1437173, 1437174 and 1437175

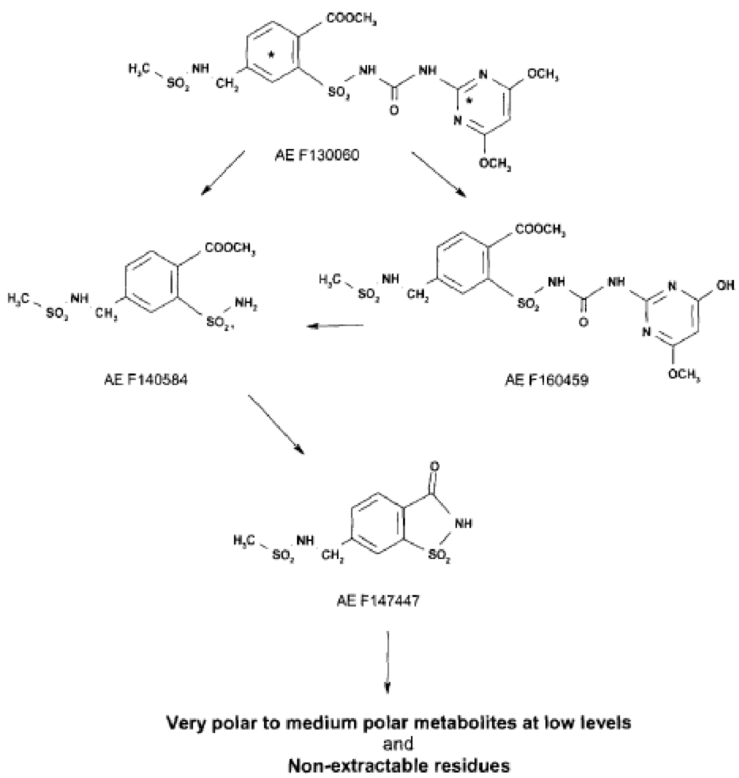


Figure 1. Metabolic Scheme of Mesosulfuron-methyl in Cereals and Rotated Crops

NATURE OF THE RESIDUE IN LAYING HEN	PMRA# 1453421

Six laying hens were orally dosed once per day for 14 consecutive days with the radiolabelled test substance at 10.24 ppm in the diet. The test animals were sacrificed ~22 hours after the final dosing period.

Total radioactivity in sample aliquots was analyzed by LSC. Identification and characterization of residues in extracts were carried out by TLC and HPLC. Metabolites were identified by co-chromatography and/or retention time comparison with reference standards. Selected purified components were analyzed by LC-MS with negative ion electron spray.

Excretion was reported to be rapid, with 82% of the AD excreted in the first 24 hours following dosing. On a daily average, 92% of the AD was found in the excreta, indicating that the dose was mostly excreted with very little of the AD available for incorporation into tissues.

TRRs (expressed as mesosulfuron-methyl equivalents) in egg yolks were detectable within 24 hours of administration of the initial dose and rose steadily to reach a plateau by Day-10 of dosing at 0.012 ppm. The TRRs in egg whites were very similar to those observed in egg yolks with a maximum of 0.011 ppm reached by Day 8 of dosing.

In edible tissues, the highest residues were observed in liver at a mean value of 0.023 ppm. Mean residues in skin, fat, and muscle were an order of magnitude lower at 0.004, ≤0.002 and <0.002 ppm, respectively.

The majority of the radioactive residues (70–85% of the TRRs) in liver, fat and eggs were extractable using organic solvents. Mesosulfuron-methyl was the major component identified in liver (22% of the TRRs, 0.005 ppm) and

NATURE OF THE RESIDUE IN LAYING HEN	PMRA# 1453421

abdominal fat (70% of the TRRs, 0.001 ppm). AE F140584, AE F160459 and AE 0195141 were identified in liver as minor metabolites (≤5% of the TRRs each, ≤0.001 ppm). No metabolites were conclusively identified in egg whites and yolks since the residue levels in the respective extracts were below the trigger value (<0.01 ppm). However, residues in the egg white extract were tentatively identified as mesosulfuron-methyl and possibly AE F147447. Residues in the egg yolk extract were tentatively identified as mesosulfuron-methyl and several minor metabolites, namely AE F160459, AE F154851 and AE F140584. The analyzes were qualitative; the metabolites characterized in the egg yolk and whites were not quantified.

The results indicate that the metabolic route in poultry proceeds by cleavage of mesosulfuron-methyl between the two rings to yield AE F140584 and subsequent isothiazole ring formation to form AE F147447. In addition, hydrolysis of a methoxy group on the pyrimidine ring of mesosulfuron-methyl yields the hydroxy metabolite AE F160459. Oxidative deamination of the parent forms the alcohol metabolite AE 0195141.

Matrices	[U-^{14}C-phenyl]	
	TRRs (ppm)	% of Administered Dose
Excreta (including cage wash)	Not reported (NR)	92.4
GI tract	0.832	NR
Liver	0.023	NR
Muscle	<0.002	NR
Abdominal fat	0.002	NR
Skin	0.004	NR
Subcutaneous fat	<0.002	NR
Undeveloped eggs	0.010	NR
Egg whites (Days 1-14)	0.133	NR
Egg yolks (Days 1-14)	0.121	NR

Metabolites identified	Major Metabolites (>10% TRR)	Minor Metabolites (<10% TRR)
Radiolabel Position	[U-^{14}C-phenyl]	[U-^{14}C-phenyl]
Liver	Mesosulfuron-methyl	AE F140584, AE F160459, AE 0195141
Abdominal Fat	Mesosulfuron-methyl	None
Egg whites	None	Tentatively identified as mesosulfuron-methyl, AE F147447
Egg yolks	None	Tentatively identified as mesosulfuron-methyl, AE F160459, AE F154851, AE F140584

NATURE OF THE RESIDUE IN LACTATING COW	PMRA # 1453422

A lactating dairy cow was orally dosed once per day for five consecutive days with the radiolabelled test substance at 20.54 ppm in the diet. The test animal was sacrificed ~22 hours after the final dosing period.

Total radioactivity in sample aliquots was analyzed by LSC. Identification and characterization of residues in extracts were carried out by TLC and HPLC. Metabolites were identified by co-chromatography and/or retention time comparison with reference standards. Selected purified components were analyzed by liquid chromatography-mass spectrometry LC-MS with positive and negative ion electro-spray.

Excretion was reported to be rapid, with 39% of the AD recovered in the feces and 2% in the urine within the first 24 hours following dosing. Excretion occurred predominantly through the fecal route with a mean daily recovery of 74% of the AD in the feces, and 4% in the urine. A further 10% of the AD was recovered in the rumen, abomasal fluid and GI contents. Residues in whole blood and plasma were very low, and appeared to plateau at 0.004 ppm in

NATURE OF THE RESIDUE IN LACTATING COW	PMRA # 1453422

blood and 0.003 ppm in plasma 48 hours after administration of initial dose, although a slightly higher magnitude of residues (0.006 ppm) were seen in plasma at 120 hours following initial dose.

TRRs (expressed as mesosulfuron-methyl equivalents) were <LOQ-0.004 ppm in milk, 0.031 ppm in liver, 0.058 ppm in kidney, 0.003–0.004 ppm in muscle and heart, 0.004–0.032 ppm in fat and 0.09 ppm in lungs. The majority of the radioactive residues were extracted using organic solvents, including 92% of the TRRs in 120-hour milk, 82% of the TRRs in liver, 83% of the TRRs in kidney, and 96% of the TRRs in renal fat. The total unextractable residues in edible tissues and milk accounted for 4–18% of the TRRs (≤0.001–0.010 ppm).

Mesosulfuron-methyl was the major component identified in all tissues (23% of the TRRs in milk, 0.001 ppm; 53% of the TRRs in liver, 0.017 ppm; 41% of the TRRs in kidney, 0.024 ppm; 20% of the TRRs in renal fat, 0.006 ppm). The cleavage products AE F140584 and AE F147447 were each identified as minor metabolites in liver (8% of the TRRs were AE F140584, 0.003 ppm; 4% of the TRRs were AE F147447, 0.001 ppm) and kidney (5% of the TRRs were AE F140584, 0.003 ppm; 6% of the TRRs were AE F147447, 0.004 ppm). The alcohol metabolite AE 0195141 was detected as a minor component in kidney (1% of the TRRs, 0.001 ppm) and a major component in renal fat (27% of the TRRs, 0.009 ppm). Metabolite AE F140584/AE F160459 was identified as a major component in milk (17% of the TRRs, 0.001 ppm).

The metabolic route in ruminants proceeds by cleavage of mesosulfuron-methyl between the two rings to yield AE F140584 and subsequent isothiazole ring formation to form AE F147447. In addition, hydrolysis of a methoxy group on the pyrimidine ring of mesosulfuron-methyl yields the hydroxy metabolite AE F160459. Oxidative deamination of mesosulfuron-methyl forms the alcohol metabolite AE 0195141.

Matrices	**[U-^{14}C-phenyl]**	
	TRRs (ppm)	**% of Administered Dose**
Urine and feces	NR	77.24
Liver	0.031	NR
Kidney	0.058	NR
Heart	0.003	NR
Lungs	0.090	NR
Muscle	0.003–0.004	NR
Fat	0.004–0.032	NR
Bile	0.605	NR
Rumen fluid	0.367	NR
Abomasal fluid	0.408	NR
GI contents	2.936	NR

Metabolites identified	**Major Metabolites (>10% TRR)**	**Minor Metabolites (<10% TRR)**
Radiolabel Position	**[U-^{14}C-phenyl]**	**[U-^{14}C-phenyl]**
Liver	Mesosulfuron-methyl	AE F140584, AE F147447
Kidney	Mesosulfuron-methyl	AE F140584, AE F147447, AE 0195141
Renal fat	Mesosulfuron-methyl, AE F0195141	None
Milk	Mesosulfuron-methyl, AE F140584/160459	None

NATURE OF THE RESIDUE IN LACTATING COW	PMRA # 1453422

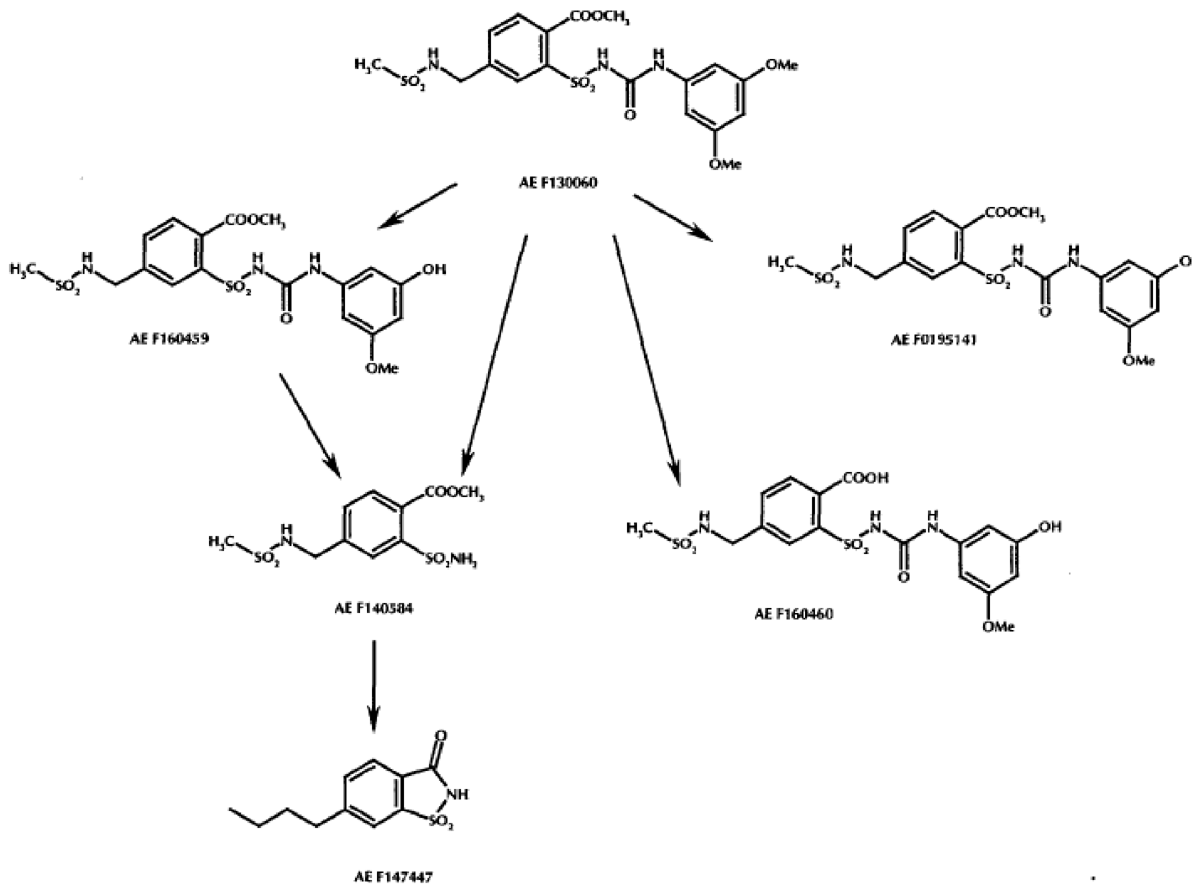


Figure 1. Metabolic Scheme of Mesosulfuron-methyl in Livestock.

CROP FIELD TRIALS ON WHEAT	PMRA #1437169, 1437163

Ten field trials on spring wheat were conducted in the US in Region 5 (4 trials), Region 7 (5 trials), and Region 11 (1 trial) during the 1998 growing season, and 14 field trials on winter wheat were conducted in the US in Region 2 (1 trial), Region 4 (1 trial), Region 5 (3 trials), Region 6 (2 trials), Region 8 (6 trials) and Region 11 (1 trial) during the 1999 growing season. At each field trial site, two separate plots were treated with mesosulfuron-methyl (75% WDG) at a target rate of 25 g a.i./ha tank-mixed with the safener AE F107892 (10% EC) at a target rate of 75 g a.i./ha. A single broadcast application of the tank mix was made to wheat either at the Zadok 30 growth stage (just prior to 1st node emergence) or at approximately 55 days prior to harvest. Broadcast applications to all plots were made with ground equipment in 42–49 L/ha of water (spring wheat trials) and in 89–100 L/ha of water (winter wheat trials), and most applications included a typical long chain alcohol surfactant (Synperonic A7) at a target rate of 400 g a.i./ha.

Spring wheat samples were harvested at PHIs of 4–24 days (forage), 14–55 days (hay) and 54–73 days (straw and grain). Winter wheat samples were harvested at PHIs of 9–68 days (forage), 34–92 days (hay), 54–57 days (straw) and 54–134 days (grain).

Commodity	Total Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT	Mean (STMR)	Median (STMdR)	Std. Dev.
Spring wheat									

CROP FIELD TRIALS ON WHEAT								PMRA #1437169, 1437163	
Forage	22	66	2	<0.05	<0.05	<0.05	0.05	<0.05	NA
Hay	22–25	66–79	18	<0.05	<0.05	<0.05	0.05	<0.05	0
Straw	22–27	66–79	20	<0.05	0.14	0.13	0.06	<0.05	0.025
Grain	22–27	66–79	20	<0.01	0.026	0.025	0.01	<0.01	0.005
Winter wheat									
Forage	24–26	73–77	24	<0.01	<0.01	<0.01	0.01	<0.01	0
Hay	24–25	73–75	12	<0.01	<0.01	<0.01	0.01	<0.01	0
Straw	24–26	73–79	40	<0.01	0.25	0.23	0.03	<0.01	0.048
Grain	24–26	73–79	40	<0.01	<0.01	<0.01	0.01	<0.01	0

RESIDUE DECLINE IN WHEAT	PMRA #1437168
No discernible trend could be observed since all treated wheat samples had residues at or below method LOQ.	

FREEZER STORAGE STABILITY	PMRA #1437164, 1437165 and 1437167
Mesosulfuron-methyl residues were shown to be stable at -18°C for up to 24 months in wheat grain and for up to 40 months in wheat shoot/forage and straw.	

PROCESSED FOOD AND FEED	PMRA #1437176
Test Site	Plots in Region 11
Treatment	Single broadcast application
Rate	78 g a.i./ha
End-use product	WDG formulation tank-mixed with safener mefenpyr-diethyl and adjuvant Synperonic A7
Preharvest interval	54 days
Processed Commodity	**Processing Factor**
Wheat flour and middlings	NA (no concentration; residues below LOQ)
Wheat bran	1.3×
Wheat shorts	1.2×
Wheat germ	4.3×
Wheat AGFs	21.6×

LIVESTOCK FEEDING	PMRA #1437177
A rationale for waiver of livestock feeding data was submitted, based on the argument that no quantifiable residues of mesosulfuron-methyl or metabolites in tissues, milk or eggs are expected at the feeding levels resulting from the use on wheat. Maximum reasonably balanced dietary burdens were calculated to be 0.23 ppm for beef cattle, 0.07 ppm for dairy cattle, 0.06 ppm for poultry and 0.06 ppm for swine. Comparison with residue levels detected in metabolism studies carried out at highly exaggerated rates showed that no quantifiable residues will occur in fat, meat, meat byproducts, milk and eggs as a result of the registration on wheat. Therefore, MRLs for these matrices are recommended at the LOQ of the enforcement method (0.01 ppm).	

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

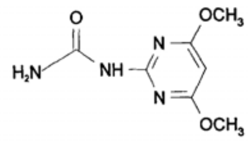
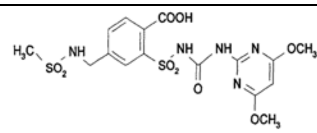
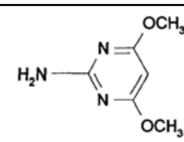
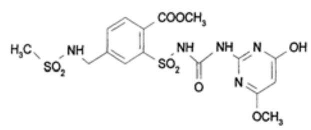
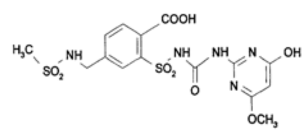
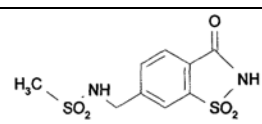
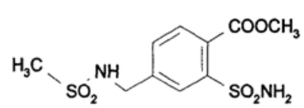
PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops (wheat)** **Rotational crops**	 Mesosulfuron-methyl Mesosulfuron-methyl
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops** **Rotational crops**	 Mesosulfuron-methyl Mesosulfuron-methyl
METABOLIC PROFILE IN DIVERSE CROPS	The profile in diverse crops cannot be determined, since only wheat was investigated.

ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT	Mesosulfuron-methyl
RESIDUE DEFINITION FOR RISK ASSESSMENT	Mesosulfuron-methyl
METABOLIC PROFILE IN ANIMALS **(cow, hen, rat)**	The metabolic profile is similar in animals investigated.
FAT SOLUBLE RESIDUE	No

DIETARY RISK FROM FOOD AND WATER

	POPULATION	ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)	
		Food Only	Food and Water
Refined chronic non-cancer dietary risk **ADI = 1.55 mg/kg bw/day** **Estimated chronic drinking water concentration = 0.88 μg/L**	**All infants <1 year**	<1	<1
	Children 1–2 years	<1	<1
	Children 3 to 5 years	<1	<1
	Children 6–12 years	<1	<1
	Youth 13–19 years	<1	<1
	Adults 20–49 years	<1	<1
	Adults 50+ years	<1	<1
	Total population	<1	<1

Table 7.1-1 Transformation Products Relevant to the Environment

CODE	CHEMICAL NAME	CHEMICAL STRUCTURE	STUDY	MAX % AR* (DAY)
F099095	2-Amino-4,6-dimethoxypyrimdine		Aerobic soil	29.2 (15)
F154851	2-[3-(4,6-Dimethoxypyrimidine-2-yl)ureidosulfonyl] -4-methanesulfonamidomethylbenzoic acid		Aerobic soil	16.2 (44)
F092944	2-Amino-4,6-dimethoxypyrimdine		Aerobic soil Hydrolysis (pH 4, 20 ºC)	10.0 (62) 34.6 (15)
F160459	Methyl 2-[3 -(4-hydroxy-6-methoxypyrimidine-2-yl)ureido-sulfonyl]-4-methanesulfonamidomethyl benzoate		Aerobic aquatic Anaerobic aquatic	21.2 17.6 (7)
F160460	2-[3-(4-Hydroxy-6-methoxypyrimidine-2-yl)ureidosulfonyl] -4-methanesulfonamidomethylbenzoic acid		Anaerobic aquatic	16 (14)
F147447	6-Methanesulfonamidomethyl-1 ,2-benzisothiazol-3 (2H)-one 1 , 1-dioxide		Hydrolysis (pH 9, 50 ºC) Aerobic aquatic	46.8 (15) 16.1 (365)
F140584	Methy1 4 -methane sulfonamidomethy1-2 -sulfamoylbenzoate		Hydrolysis (pH 4, 30ºC)	50.3 (5)

* AR, applied radioactivity.

Table 7.1-2 Fate and Behaviour of Mesosulfuron-methyl and Its Transformation Products in the Environment

Property	Test substance	Value	Transformation products*	Comments
Abiotic transformation				
Hydrolysis	[^{14}C]-2-pyr-F130060 and [^{14}C]-U-phen-F130060	pH 4: t½ 3.5 d pH 7: stable pH 9: stable	F154851; **F092944**; F147447; **F140584**	major route of transformation under acidic conditions; stable at neutral and alkaline conditions
Phototransformation on soil	[^{14}C]-2-pyr-F130060 and [^{14}C]-U-phen-F130060	stable	None	Not major route of transformation in the environment

Property	Test substance	Value	Transformation products*	Comments
Biotransformation				
Biotransformation in aerobic soil	[14C]-2-pyr-F130060 and [14C]-U-phen-F130060	DT_{50}: 8.56–74.8 d (SFO) DT_{90}: 28.4–887 d (SFO/DFOP)	**F099095**; **F154851**; **F092944**; F160459; F160460; F147447; F140584;	Non-persistent to moderately persistent Major route of transformation
Biotransformation in anaerobic soil	[14C]-2-pyr-F130060 and [14C]-U-phen-F130060	DT_{50}: 26.8 d (SFO) DT_{90}: 89.1 d (SFO)	**F160459**; F160460; F092944; F154851; F099095	Slightly persistent Maybe a major route of transformation.
Mobility				
Adsorption / desorption in soil	[14C]-2-pyr-F130060 [14C]-2-phen-F154851 [14C]-2-pyr-F099095	Ads K_d: 0.37–3.56 mL/g; K_{oc}: 24-298 mL/g Ads K_d: 0.71–3.09 mL/g; K_{oc}: 44-98 mL/g Ads K_d: 2.19–69.04 mL/g; K_{oc}: 134-2192 mL/g		Slightly to highly mobile
Soil leaching	no data were submitted; these data are not required as data on adorption/ desorption were submitted			
Volatilization	no data were submitted; these data are not required as this product is non-volatile based on low values of VP and HLC			
Field studies				
Field dissipation	F130060 WDG (END-USE PRODUCT)	DT_{50}: 13.6 d DT_{90}: 45.2 d	Not measured	Non-persistent
Field leaching	F130060 WDG (END-USE PRODUCT)	no residues beyond 30 cm soil depth	Not measured	Low leaching potential

Legend: See Table.4.1-1

Table 7.2-1 Toxicity to Non-target Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity	PMRA #
Terrestrial organisms					
Earthworm (*Eisenia fetida)*	14 d-Acute	F130060	LC_{50}: >1000 mg a.i./kg dw soil NOEC: 1000 mg a.i./kg dw soil EC_{50}: >1000 mg a.i./kg dw soil	NA	1453465
Honeybees (*Apis mellifera* L.)	72 h-Acute oral	F130060	LD_{50}: >184.8 μg a.i./bee	Relatively non-toxic	1453368
	72 h-Acute contact	F130060	LD_{50}: >13 μg a.i./bee NOAEL: 13 μg a.i./bee		1453367
Bobwhite quail (*Colinus viriginianus*)	Acute oral	F130060	LD_{50}: >2000 mg a.i./kg bw NOAEL: 2000 mg a.i./kg bw	Practically non-toxic	1453476
	5 d-Acute dietary	F130060	LC_{50}: >4800 mg a.i./kg diet LD_{50}: >720.0 mg a.i./kg bw/day NOEC: 4800 mg a.i./kg diet	Slightly toxic	1453379
	20 w-Reproduction	F130060	NOEC: 1000 mg a.i./kg diet (highest concentration tested)		1453381

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity	PMRA #
Maillard duck (*Anas platyrhynchos*)	Acute oral	F130060	LD_{50}: >2000 mg a.i./kg bw NOAEL: 2000 mg a.i./kg bw	Practically non-toxic	1453378
	5 d-Acute dietary	F130060	LC_{50}: >4750 mg a.i./kg diet LD_{50}: >126 mg a.i./kg bw/day NOEC: 309 mg a.i./kg diet (based on feed consumption)	Slightly toxic	1453380
	21 w-Reproduction	F130060	NOEC: 990 mg a.i./kg diet (highest concentration tested)	NA	1453381
Rat, Wistar	Acute oral	F130060	LD_{50}: >5000 mg a.i./kg bw /day	NA	1761883
	90 d-Dietary	F130060	NOAEL: 908 mg a.i./kg bw/day	NA	1761883
Rat, Sprague-Dawley	Reproduction (multi-generation)	F130060	NOAEL: 1175 mg a.i./kg bw/day	NA	1761883
Vascular plant	14 d-Seedling emergence	F130060 AE F107892	**Monocot**, most sensitive: onion (shoot length) EC_{25}: 8.4 g a.i./ha **Dicot**: most sensitive: Lettuce (shoot length) EC_{25}: 6.0 g a.i./ha	NA	1453389
	14 d-Vegetative vigour	F130060 AE F107892	**Monocot**, most sensitive: Corn (dry weight) EC_{25}: 0.47 g a.i./ha **Dicot**: most sensitive: Tomato (dry weight) EC_{25}: 0.18 g a.i./ha	NA	1453390
	HR_5 of SSD of EC_{50}: 0.3494 g a.i./ha			NA	1790314
Aquatic organisms					
Rainbow trout (*Oncorhynchus mykiss)*	96 h-Acute	F130060	LC_{50} was >91.5 mg a.i./L. NOEC: 91.5 mg a.i./L EC_{50} >91.5 mg a.i./L	Slightly toxic	1453374
	Subchronic	F130060	LC_{50} >29.6 mg a.i./L NOEC: 29.6 mg a.i./L.		1453377
	ELS	F130060	Data not submitted		
Bluegill sunfish *(Lepomis macrochirus*)	96 h-Acute	F130060	LC_{50} >96.4 mg a.i./L NOEC: 96.4 mg a.i./L LOEC >96.4 mg a.i./L	Slightly toxic	1453375
Daphnia *(Daphnia magna)*	48 h-Acute	F130060	EC_{50} >90.2 mg a.i./L LOEC >90.2 mg a.i./L NOEC: 90.2 mg a.i./L	Slightly toxic	1453369
	21 d-Chronic	F130060	NOAEC: 1.7 mg a.i./L (dry weight) LC/EC_{50} >90.0 mg a.i./L		1453370 1453371
Freshwater blue-green algae *(Anabaena flos-aquae)*	96 h-Acute	F130060	NOAEC: 1.1 mg a.i./L EC_{50} : 2.4 mg a.i./L (cell density and biomass)		1453385

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity	PMRA #
Freshwater green algae (*Pseudokirchneriella subcapitata)*	96 h-Acute	F130060	NOAEC: 0.029 mg a.i./L EC_{05}: 0.11 mg a.i./L EC_{50}: 0.21 mg a.i./L (biomass)		1453386
	96 h-Acute	F160459	NOAEC : 54.6 mg a.i./L EC_{50}: 98.4 mg a.i./L (biomass)		1453383
	96 h-Acute	F147447	NOAEC: 92.0 mg a.i./L EC_{50} >92.0 mg a.i./L (biomass)		1453387
Freshwater diatom *(Navicula pelliculosa)*	96 h-Acute	F130060	NOAEC: 70.8 mg a.i./L EC_{50} >70.8 mg a.i./L (biomass)		1453384
Duckweed (*Lemna gibba*)	7 d-Dissolved	F130060	NOEC: 0.00019 mg a.i./L (frond number) EC_{50}: 0.00064 mg a.i./L (frond number)		1453391
	7 d-Dissolved	F160460	NOEC: 94.71 mg a.i./L EC_{50} >94.71 mg a.i./L		1453392
	7 d-Dissolved	F160459	NOEC: 0.29 mg a.i./L (frond number) EC_{50}: 1.5 mg a.i./L (frond number)		1453393
	7 d-Dissolved	F147447	NOEC: 90.33 mg a.i./L EC_{50} >90.33 mg a.i./L		1453394
Sheepshead minnow (*Cyprinodon variegatus*)	96 h-Acute	F130060	LC_{50} >105 mg a.i./L NOEC: 105 mg a.i./L LOEC >105 mg a.i./L	Practically non-toxic	1453376
Eastern oyster (*Crassostrea virginica)*	96 h-Acute	F130060	EC_{50} >100 mg a.i./L. NOEC: 100 mg a.i./L	Practically non-toxic	1453373
Saltwater mysid (*Americamysis bahia*)	96 h-Acute	F130060	LC_{50} >111 mg a.i. /L NOEC: 111 mg a.i. /L	Practically non-toxic	1453372
Saltwater diatom *(Skeletonema costatum)*	96 h-Acute	F130060	EC_{50}: 98 mg a.i./L (Biomass) NOAEC: 37.8 mg a.i./L		1453388

Legend: See Table.4.1-1

Table 7.2-2 Endpoints Used for Risk Assessment and the Uncertainty Factors Applied

Taxonomic group	Exposure	Endpoint	Uncertainty Factor
Earthworm	Acute	LC_{50}	0.5
	Chronic	NOEC	1.0
Bees	Acute	LD_{50}	1.0
Other non-target arthropods	Acute	LR_{50}	1.0
Birds	Acute oral	LD_{50}	0.1
	Dietary	LD_{50}	0.1
	Reproduction	NOEL	1.0
Mammals	Acute oral	LD_{50}	0.1
	Reproduction	NOEL	1.0

Taxonomic group	Exposure	Endpoint	Uncertainty Factor
Non-target terrestrial plants	Acute	HR_5 of SSD of ER_{50}[5]	1.0
Aquatic invertebrates	Acute	EC_{50}	0.5
	Chronic	NOEC	1.0
Fish	Acute	LC_{50}	0.1
	Chronic	NOEC	1.0
Amphibians	Acute	Fish LC_{50}	0.1
	Chronic	Fish NOEC	1.0
Algae	Chronic	EC_{50}	0.5
Aquatic vascular plants	Chronic	EC_{50}	0.5

Table 7.2-3 Screening Level Risk Assessment on Non-Target Species

Table 7.2-3a Risk to Terrestrial Organisms Other Than Birds and Mammals					
Organism	**Exposure**	**Endpoint value**	**EEC**	**RQ[1]**	**Level of concern exceeded[1]**
Invertebrates					
Earthworm	Acute	LC_{50}/10: >500 mg a.i./kg soil	0.0011 mg a.i./kg soil	<0.000002	No
Bee	Oral	LD_{50}: >207 kg a.i./ha	0.0025 kg a.i./ha	<0.000012	No
	Contact	LD_{50}: >14.56 kg a.i./ha	0.0025 kg a.i./ha	<0.00017	No
Vascular plants					
Vascular plant	Vegetative vigour	HR_5 = 0.349 g a.i./ha	2.5 g a.i./ha	7.15	Yes

[1]RQ = exposure / toxicity; shaded cells indicate that the screening level RQ exceeds the LOC (1.0).

Table 7.2-3b Risk to Birds and Mammals					
Exposure type	**Toxicity endpoint (mg a.i./kg bw/d)**	**Food guild**	**On-field**		
			EDE (mg a.i./kg bw)	**RQ**	**LOC exceeded**
Small bird (0.02 kg)					
Acute	>200	Insectivore (small insects)	0.1260	<0.0006	No
	>200	Granivore (grain and seeds)	0.0315	<0.0002	No
	>200	Frugivore (fruit)	0.0630	<0.0003	No
Dietary	>72	Insectivore (small insects)	0.1260	<0.0017	No
	>72	Granivore (grain and seeds)	0.0315	<0.0004	No
	>72	Frugivore (fruit)	0.0630	<0.0009	No
Reproduction	93	Insectivore (small insects)	0.1260	0.0014	No
	93	Granivore (grain and seeds)	0.0315	0.0003	No
	93	Frugivore (fruit)	0.0630	0.0007	No
Medium sized bird (0.1 kg)					
Acute	>200	Insectivore (small insects)	0.0983	<0.0005	No
	>200	Insectivore (large insects)	0.0246	<0.0001	No
	>200	Granivore (grain and seeds)	0.0246	<0.0001	No
	>200	Frugivore (fruit)	0.0492	<0.0002	No
Dietary	>72	Insectivore (small insects)	0.0983	<0.0014	No
	>72	Insectivore (large insects)	0.0246	<0.0003	No
	>72	Granivore (grain and seeds)	0.0246	<0.0003	No
	>72	Frugivore (fruit)	0.0492	<0.0007	No
Reproduction	93	Insectivore (small insects)	0.0983	0.0011	No
	93	Insectivore (large insects)	0.0246	0.0003	No
	93	Granivore (grain and seeds)	0.0246	0.0003	No

[5] 5th percentile hazard rate of the species sensitivity distribution of ER50 values

Table 7.2-3b Risk to Birds and Mammals

Exposure type	Toxicity endpoint (mg a.i./kg bw/d)	Food guild	On-field		
			EDE (mg a.i./kg bw)	RQ	LOC exceeded
	93	Frugivore (fruit)	0.0492	0.0005	No
Large sized bird (1 kg)					
Acute	>200	Insectivore (small insects)	0.0287	<0.0001	No
	>200	Insectivore (large insects)	0.0072	<0.0000	No
	>200	Granivore (grain and seeds)	0.0072	<0.0000	No
	>200	Frugivore (fruit)	0.0144	<0.0001	No
	>200	Herbivore (short grass)	0.1026	<0.0005	No
	>200	Herbivore (long grass)	0.0626	<0.0003	No
	>200	Herbivore (forage crops)	0.0949	<0.0005	No
	>200	Herbivore (leafy foliage)	0.1933	<0.0010	No
Dietary	>72	Insectivore (small insects)	0.0287	<0.0004	No
	>72	Insectivore (large insects)	0.0072	<0.0001	No
	>72	Granivore (grain and seeds)	0.0072	<0.0001	No
	>72	Frugivore (fruit)	0.0144	<0.0002	No
	>72	Herbivore (short grass)	0.1026	<0.0014	No
	>72	Herbivore (long grass)	0.0626	<0.0009	No
	>72	Herbivore (forage crops)	0.0949	<0.0013	No
	>72	Herbivore (leafy foliage)	0.1933	<0.0027	No
Reproduction	93	Insectivore (small insects)	0.0287	0.0003	No
	93	Insectivore (large insects)	0.0072	0.0001	No
	93	Granivore (grain and seeds)	0.0072	0.0001	No
	93	Frugivore (fruit)	0.0144	0.0002	No
	93	Herbivore (short grass)	0.1026	0.0011	No
Small mammal (0.015 kg)					
Acute	>500	Insectivore (small insects)	0.0725	<0.0001	No
	>500	Granivore (grain and seeds)	0.0181	<0.0000	No
	>500	Frugivore (fruit)	0.0362	<0.0001	No
Dietary	908	Insectivore (small insects)	0.0725	0.0001	No
	908	Granivore (grain and seeds)	0.0181	0.0000	No
	908	Frugivore (fruit)	0.0362	0.0000	No
Reproduction	1175	Insectivore (small insects)	0.0725	0.0001	No
	1175	Granivore (grain and seeds)	0.0181	0.0000	No
	1175	Frugivore (fruit)	0.0362	0.0000	No
Medium sized mammal (0.035 kg)					
Acute	>500	Insectivore (small insects)	0.0635	<0.0001	No
	>500	Insectivore (large insects)	0.0159	<0.0000	No
	>500	Granivore (grain and seeds)	0.0159	<0.0000	No
	>500	Frugivore (fruit)	0.0318	<0.0001	No
	>500	Herbivore (short grass)	0.2270	<0.0005	No
	>500	Herbivore (long grass)	0.1386	<0.0003	No
	>500	Herbivore (forage crops)	0.2100	<0.0004	No
	>500	Herbivore (leafy foliage)	0.4278	<0.0009	No
Dietary	908	Insectivore (small insects)	0.0635	0.0001	No
	908	Insectivore (large insects)	0.0159	0.0000	No
	908	Granivore (grain and seeds)	0.0159	0.0000	No
	908	Frugivore (fruit)	0.0318	0.0000	No
	908	Herbivore (short grass)	0.2270	0.0002	No
	908	Herbivore (long grass)	0.1386	0.0002	No
	908	Herbivore (forage crops)	0.2100	0.0002	No
	908	Herbivore (leafy foliage)	0.4278	0.0005	No
Reproduction	1175	Insectivore (small insects)	0.0635	0.0001	No
	1175	Insectivore (large insects)	0.0159	0.0000	No
	1175	Granivore (grain and seeds)	0.0159	0.0000	No
	1175	Frugivore (fruit)	0.0318	0.0000	No
	1175	Herbivore (short grass)	0.2270	0.0002	No

Table 7.2-3b Risk to Birds and Mammals					
Exposure type	**Toxicity endpoint (mg a.i./kg bw/d)**	**Food guild**	**On-field**		
			EDE (mg a.i./kg bw)	**RQ**	**LOC exceeded**
	1175	Herbivore (long grass)	0.1386	0.0001	No
	1175	Herbivore (forage crops)	0.2100	0.0002	No
	1175	Herbivore (leafy foliage)	0.4278	0.0004	No
Large sized mammal (1 kg)					
Acute	>500	Insectivore (small insects)	0.0339	<0.0001	No
	>500	Insectivore (large insects)	0.0085	<0.0000	No
	>500	Granivore (grain and seeds)	0.0085	<0.0000	No
	>500	Frugivore (fruit)	0.0170	<0.0000	No
	>500	Herbivore (short grass)	0.1213	<0.0002	No
	>500	Herbivore (long grass)	0.0741	<0.0001	No
	>500	Herbivore (forage crops)	0.1122	<0.0002	No
	>500	Herbivore (leafy foliage)	0.2286	<0.0005	No
Dietary	908	Insectivore (small insects)	0.0339	0.0000	No
	908	Insectivore (large insects)	0.0085	0.0000	No
	908	Granivore (grain and seeds)	0.0085	0.0000	No
	908	Frugivore (fruit)	0.0170	0.0000	No
	908	Herbivore (short grass)	0.1213	0.0001	No
	908	Herbivore (long grass)	0.0741	0.0001	No
	908	Herbivore (forage crops)	0.1122	0.0001	No
	908	Herbivore (leafy foliage)	0.2286	0.0003	No
Reproduction	1175	Insectivore (small insects)	0.0339	0.0000	No
	1175	Insectivore (large insects)	0.0085	0.0000	No
	1175	Granivore (grain and seeds)	0.0085	0.0000	No
	1175	Frugivore (fruit)	0.0170	0.0000	No
	1175	Herbivore (short grass)	0.1213	0.0001	No
	1175	Herbivore (long grass)	0.0741	0.0001	No
	1175	Herbivore (forage crops)	0.1122	0.0001	No
	1175	Herbivore (leafy foliage)	0.2286	0.0002	No

Table 7.2-3c Risk to Aquatic Organisms						
Organism	**Exposure**	**Test substance**	**Endpoint value (mg a.i. or TP/L)**	**EEC (mg a.i. or TP/L)**	**RQ**	**Level of concern exceeded**
Freshwater species						
Daphnia magna	Acute	F130060	EC_{50}÷ 2 >45.1	0.0003125	<0.000007	No
	Chronic	F130060	NOEC = 1.7	0.0003125	<0.00018	No
Rainbow trout	Acute	F130060	LC_{50}÷ 10 >9.15	0.0003125	<0.000034	No
Bluegill sunfish	Acute	F130060	LC_{50}÷ 10 >9.64	0.0003125	<0.000032	No
Amphibians	Acute	F130060	LC_{50}÷ 10 >9.15 (most sensitive fish)	0.0016	<0.000175	No
Blue-green algae	Acute	F130060	EC_{50}÷ 2 = 1.2	0.0003125	0.000260	No
Green algae	Acute	F130060	EC_{50}÷ 2 = 0.1	0.0003125	0.003130	No
		F160459	EC_{50}÷ 2 = 49.2	0.00030375	0.000006	No
		F147447	EC_{50}÷ 2 >46	0.00018	<0.000004	No
Diatom	Acute	F130060	EC_{50}÷ 2 >35.4	0.0003125	<0.000009	No
Vascular plant: Duckweed	Dissolved	F130060	EC_{50}÷ 2 = 0.00032	0.0003125	0.977000	No
		F160460	EC_{50}÷ 2 >47.3	0.000295	<0.000006	No
		F160459	EC_{50}÷ 2 = 0.75	0.00030375	0.000405	No
		F147447	EC_{50}÷ 2 >45.2	0.00018	<0.000004	No

Table 7.2-3c Risk to Aquatic Organisms						
Organism	**Exposure**	**Test substance**	**Endpoint value (mg a.i. or TP/L)**	**EEC (mg a.i. or TP/L)**	**RQ**	**Level of concern exceeded**
Marine species						
Crustacean (mysid)	Acute	F130060	EC_{50}÷ 2 >55.5	0.0003125	<0.000006	No
Mollusk (Eastern oyster)	Acute	F130060	EC_{50}÷ 2 >50	0.0003125	<0.000006	No
Sheephead minnow	Acute	F130060	LC_{50}÷ 10 >10.5	0.0003125	<0.002980	No
Marine diatom	Acute	F130060	EC_{50}÷ 2= 49	0.0003125	0.000006	No

Table 8 Toxic Substances Management Policy Considerations-Comparison to Toxic Substances Management Policy

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints	Transformation Products (TP) Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes	Yes [a]
Predominantly anthropogenic[2]	Yes		Yes	Yes
Persistence[3]:	Soil	Half-life ≥182 days	DT_{50} 8.56–74.8 days	Most of TP are not expected to be persistent [b]
	Water	Half-life ≥182 days	DT_{50} 24.8–77.3 days	
	Sediment	Half-life ≥365 days	DT_{50} 7.24 days (anaerobic aquatic)	
	Air	Half-life ≥2 days or evidence of long range transport	Half-life or volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure (3.5×10^{-12} Pa at 20°C) and Henry's law constant (K= 3.6×10^{-17} atm.m^{3}·mol^{-1}).	Not available
Bioaccumulation[4]	Log K_{OW} ≥5		0.331	Not available
	Bioconcentration factor ≥5000		Not available	Not available
	Bioaccumulation factor ≥5000		Not available	Not available
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.	No, does not meet TSMP Track 1 criteria.
[1]All pesticides will be considered toxic or toxic-equivalent according to the *Canadian Environmental Protection Act* for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the *Canadian Environmental Protection Act* toxicity criteria may be refined if required (in other words, all other TSMP criteria are met).				

TSMP Track 1 Criteria	TSMP Track 1 Criterion value	Active Ingredient Endpoints	Transformation Products (TP) Endpoints
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgment, 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) meets one persistence criterion identified for one media (soil, water, sediment or air) then the criterion for persistence is considered to be met. [4]Field data (for example, bioaccumulation factors) are preferred over laboratory data (for example, bioaccumulation factors) which, in turn, are preferred over chemical properties (for example, log K_{OW}).			

[a] Only TP **F160459** exhibited herbicidal effects to aquatic plants.
[b] In soil and aquatic biotransformation studies, the levels of major TP reached maximum within 60 days, then rapidly declined to <50% within 180 days post-treatment. It should be noted, however, that the persistence of F147447 is not known, since this transformation product increased until study termination.

Table 9 Alternative Herbicides for Wild Oats Control in Spring and/or Durum Wheat

Technical Grade Active Ingredient	End-use Products	Weed Claims	Herbicide Classification	
			Group	Mode of Action
flucarbazone	Everest	**controls:** wild oats, green foxtail, volunteer tame oats, redroot pigweed, wild mustard, stinkweed, volunteer canola, green smartweed, and shepherd's purse	2	ALS inhibitor
imazamethabenz	Assert	**controls:** wild oats, wild mustard, and stinkweed **suppresses**: wild buckwheat and tartary buckwheat	2	ALS inhibitor
sulfosulfuron	Sundance (soil restrictions)	**controls:** wild oats, foxtail barley, common chickweed, wild mustard, redroot pigweed, stinkweed, volunteer canola, cleavers **suppresses:** green foxtail, quackgrass, barnyardgrass, dandelion, perennial sow-thistle	2	ALS inhibitor
thifensulfuron methyl + fenoxaprop + MCPA	Triumph Plus (spring wheat only)	wild oats, green foxtail, yellow foxtail and several broadleaf weeds	2, 1, & 4	ALS inhibitor, ACCase inhibitor & synthetic auxin
fenoxaprop-p-ethyl + bromoxynil + MCPA	Puma One Pass Postemergent Herbicide Tank Mix	wild oats, green foxtail, barnyard grass & many broadleaf weeds (including perennials)	1, 6, & 4	ACCase inhibitor, photosynthesis inhibitor at PSII & synthetic auxin
tralkoxydim + clopyralid + MCPA	Prevail Liquid Herbicide Tank Mix	annual grasses and broadleaf weeds	1, 4, & 4	ACCase inhibitor & synthetic auxins
clodinafop + MCPA + dicamba	Bounty Tank-Mix	annual grasses and broadleaf weeds	1, 4, & 4	ACCase inhibitor & synthetic auxin
clodinafop-propargyl	Horizon	annual grasses only	1	ACCase inhibitor
tralkoxydim	Achieve, Affirm	annual grasses only	1	ACCase inhibitor
diclofop-methyl	Hoe-Grass 284	annual grasses only	1	ACCase inhibitor
clodinafop-propargyl	Horizon	annual grasses only	1	ACCase inhibitor
fenoxaprop-p-ethyl	Puma Super	annual grasses only	1	ACCase inhibitor
pinoxaden	Axial	annual grasses only	1	ACCase inhibitor

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

Canadian MRLs are the same as those in the US. No Codex MRLs have been established.

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