PRD2008-05

Proposed Registration Decision

Foramsulfuron Technical Herbicide

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Overview

Proposed Registration Decision for Foramsulfuron and End-Use Products Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing conversion from conditional to full registration of the technical grade active ingredient foramsulfuron and end-use product Option 35 DF Herbicide for control of certain broadleaf and grassy weeds in field corn in Eastern Canada and Manitoba.

An evaluation of available scientific information found that, under the approved conditions of use, Option 35 DF Herbicide has value and does not present an unacceptable risk to human health or the environment.

End-use product Option 2.25 OD Liquid Herbicide will remain a conditional registration until the remaining data requirements have been addressed.

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 foramsulfuron and Option 35 DF Herbicide.

What Does Health Canada Consider When Making a Registration Decision?

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

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

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

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

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

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

What Is Foramsulfuron?

Foramsulfuron is the active ingredient in the herbicide end-use products, Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide. These end-use products are applied after the weeds emerge (post-emergent) and will provide control of specific broadleaf weeds and grasses in field corn.

Health Considerations

Can Approved Uses of Foramsulfuron Affect Human Health?

Foramsulfuron is unlikely to affect your health when used according to the proposed label directions.

Potential exposure to foramsulfuron may occur through diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is expected to be well below levels that cause no anticipated 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

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

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

much higher) than levels to which humans are normally exposed when using foramsulfuron products according to label directions.

Foramsulfuron does not require any further label statements as there were no significant effects on animals during acute testing. End-use product Option 2.25 OD Liquid Herbicide caused moderate dermal irritation and was a skin sensitizer. Consequently, the label statement "Warning—Skin Irritant and Potential Skin Sensitizer" is required. The other formulation, Option 35 DF Herbicide, caused moderate dermal irritation, mild eye irritation and was a skin sensitizer. As a result, the following label statement is required: "Warning—Skin and Eye Irritant and Potential Skin Sensitizer."

Foramsulfuron did not cause cancer in animals and the weight of evidence indicates it is not genotoxic. There was also no indication that foramsulfuron caused damage to the nervous system and there were no effects on reproduction. Foramsulfuron is of low toxicity over long periods and did not demonstrate any effects on any organs at the highest dose tested. The risk assessment used the highest dose tested in the chronic studies, where no effects were observed. No endpoints of concern were noted. However, the risk assessment protects against potential effects by ensuring that the level of human exposure is well below the dose at which no effects were found.

When foramsulfuron was given to pregnant animals, no effects were observed on the mothers, the developing fetus or the young animals. This indicates that the fetus and young animals were not more sensitive than the mothers and specific protection is not required in the risk assessment.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary risk estimates (food and water) revealed that the general population and infants, the subpopulation that would ingest the most foramsulfuron relative to body weight, are expected to be exposed to negligible risk levels (i.e. much less than 1% of the acceptable daily intake). Based on these estimates, the chronic dietary risk from foramsulfuron is not of concern for all population subgroups.

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

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.

Field corn residue trials conducted throughout Canada and the United States using foramsulfuron were acceptable. The MRL for field corn grain can be found in the Appendix II of this consultation document.

Occupational Risks From Handling Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide

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

Farmers and pesticide applicators mixing, loading or applying Option 35 DF Herbicide or Option 2.25 OD Liquid Herbicide, as well as field workers re-entering freshly treated fields, can come in direct contact with foramsulfuron on the skin or through inhalation of spray mists. Therefore, the label specifies that anyone mixing/loading, applying or involved in clean-up or repair activities with Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide must wear a long-sleeved shirt, long pants, socks and footwear and that anyone mixing/loading or involved in clean-up or repair activities must also wear chemical-resistant gloves. Considering these label requirements and that occupational exposure is expected to be brief because this herbicide is applied only once per year, risk to farmers, applicators or workers is not a concern.

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

Environmental Considerations

What Happens When Foramsulfuron Is Introduced Into the Environment?

Foramsulfuron is toxic to terrestrial plants. While foramsulfuron is not toxic to fish and aquatic organisms, the end-use products (Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide) have been found to be toxic to aquatic vascular plants. Therefore, buffer zones are required during application.

Foramsulfuron enters the environment when used as a herbicide on corn. Foramsulfuron is non-persistent in soil, slightly persistent in water and moderately persistent in sediment, while the major breakdown product is non-persistent in soil. Foramsulfuron is very mobile in soil and may leach to groundwater. The major breakdown product was found to be mobile in loamy sand, but immobile in silt loam. Based on its low volatility, foramsulfuron residues are not expected in the air.

Foramsulfuron and its major breakdown product present a low risk to wild mammals, birds, earthworms, bees and other arthropods, aquatic invertebrates, fish, algae and aquatic plants. However, the end-use products were found to be a risk to terrestrial and aquatic plants. Therefore, a buffer zone of one metre is required for aquatic habitats for both Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide. For terrestrial

environments, a buffer zone of 10 metres is required for Option 35 DF Herbicide and three metres for Option 2.25 OD Liquid Herbicide.

Foramsulfuron and its end-use products had been granted conditional registration with additional information required regarding the log K_{ow} for the transformation products of foramsulfuron, the log K_{ow} for the transformation products of the safener, and the toxicity of the end-use products Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide to aquatic vascular plants. The additional information was provided. However, the toxicity of Option 2.25 OD Liquid Herbicide to aquatic vascular plants is still unknown. Therefore, full registration cannot be granted for this end-use product at this time.

Value Considerations

What is the Value of Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide?

Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide, postemergence herbicides, control both grasses and broadleaf weeds in field corn.

A single application of Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide provides effective control of a range of broadleaf and grassy weeds in field corn. It is also compatible with integrated weed management practices and conventional crop production systems. Since both end-use products are applied after weeds have emerged, farmers can better assess whether the herbicide is necessary or suitable for particular weed species.

Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide had been granted conditional registration with one of the conditions being that the lowest effective rate for lambsquarters, yellow foxtail, large crabgrass, barnyard grass and bristly foxtail be established. The registrant provided additional data to support the rate of 35 g a.i./ha for each of these weed species. The condition of registration has now been adequately addressed from a value perspective and no further data are required.

Measures to Minimize Risk

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

Key risk-reduction measures being proposed on the label of Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk Reduction Measures

- **Human Health**

Since there is a concern with users coming into direct contact with foramsulfuron on the skin or through inhalation of spray mists, anyone mixing/loading, applying or involved in clean-up or repair activities with Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide must wear a long-sleeved shirt, long pants, socks and footwear, and anyone mixing/loading or involved in clean-up or repair activities must also wear chemical-resistant gloves.

- **Environment**

A buffer zone of one metre is required for aquatic habitats for both Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide. For terrestrial environments, a buffer zone of 10 metres is required for Option 35 DF Herbicide and three metres for Option 2.25 OD Liquid Herbicide.

Next Steps

Before making a final registration decision to convert the technical grade active ingredient, foramsulfuron, and end-use product Option 35 DF Herbicide from a conditional to full registration, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Registration Decision document, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments. The other end-use product, Option 2.25 OD Liquid Herbicide, will remain conditionally registered until the outstanding data requirements are addressed.

Other Information

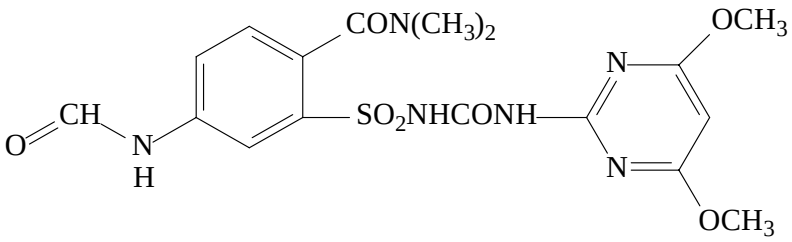
At the time the PMRA makes its registration decision, it will publish a Registration Decision document on foramsulfuron (based on the Science Evaluation of this consultation document and Regulatory Note REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*). In addition, only 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

Foramsulfuron

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Technical Grade Active Ingredient

Active ingredient		Foramsulfuron
Function		Herbicide
Chemical name		
1.	International Union of Pure and Applied Chemistry (IUPAC)	1-(4,6-dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)-5-formamidophenylsulfonyl]urea
2.	Chemical Abstracts Service (CAS)	2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-4-(formylamino)-N,N-dimethylbenzamide
CAS Number		173159-57-4
Molecular formula		$C_{17}H_{20}N_6O_7S$
Structural formula		
Molecular weight		452.49
Purity of the technical grade active ingredient		98.8% nominal (limits: 96.0%–100.0%)

Refer to Regulatory Note REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*, for a detailed chemical assessment of Foramsulfuron Technical and a detailed assessment of the value of the end-use products, Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide.

2.0 Methods of Analysis

2.1 Methods for Residue Analysis

A high-performance liquid chromatography method with UV detection was developed for the determination of foramsulfuron and a gas chromatography (GC) method with mass spectrometry (MS) detection for its metabolite AE F092944 in soil samples. A high-performance liquid chromatography method with tandem mass spectrometry (HPLC-MS/MS) was developed for foramsulfuron and its metabolite AE F153745 in sediment. A solvent gradient HPLC/UV method was provided for the determination of the parent compound and an LC/MS/MS method for the parent compound and its metabolite AE F130619 in drinking water and in surface water. Two LC/MS/MS methods were provided for the determination of the parent compound and its metabolite AE F153745 in an animal matrix.

These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limits of quantitation. Acceptable recoveries (70–120%) were obtained in animal matrices and environmental media. Based on the validation data, the methods were accepted for use as post registration monitoring methods. Methods for residue analysis are summarized in Appendix I, Table 1.

Refer to Regulatory Note REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*, for a detailed assessment of the methods of residue analysis of Foramsulfuron Technical.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The Pest Management Regulatory Agency (PMRA) conducted a detailed review of the toxicological database for foramsulfuron. The database is complete, consisting of the full array of laboratory animal (in vivo) and cell culture (in vitro) toxicity studies currently required for health hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to characterize the toxicity of this pest control product.

In rats, absorption of orally administered [^{14}C-phenyl] foramsulfuron at doses of 10 or 1000 mg/kg bw was limited (approximately 20%), with rapid elimination. Maximum concentrations in the blood were attained within one to four hours of dosing for the low- and high-dose groups, respectively. The $t_{1/2}$ for elimination from the plasma was 5.4 and 18.5 hours in low-dose females and males, respectively, and 2.4–2.9 hours for high-dose rats. The primary route of excretion was via the feces; 86.8–97.1% of the dose was excreted in the feces and 5.1–5.8% in the urine in the low-dose group and 1.3–1.5% in the urine in the high-dose group within three days of dosing. In a 14-day repeat dose experiment, fecal excretion accounted for 61.0% in males and 88.8% in females. This sex-related difference was attributed to a substantial amount of radioactivity remaining in the carcass/gastrointestinal tract of males (24.5%)

compared to females (3.1%) at sacrifice (2 days postdosing). In bile duct-cannulated rats, fecal excretion accounted for 75.6% of the dose, while urinary and bile excretion accounted for 12.7% and 4.2%, respectively.

The low levels of urinary and biliary excretion in the low-dose rats and the reduced level of urinary excretion in the high-dose rats indicated that absorption of [^{14}C-phenyl] foramsulfuron was limited. Maximum concentrations of [^{14}C-phenyl] foramsulfuron were observed 0.5–4 hours postdosing, with the exception of the thyroid and adrenals in the high-dose group. Average concentrations of radioactivity were ≤0.003 µg/g in all tissues from low-dose animals and ranged from below background to 78.7 µg/g in tissues from high-dose animals 72 hours postdosing. The relative distribution in tissues was similar for both sexes and dose groups, with the highest concentrations found in the liver, kidney, thyroid and adrenals (high-dose only). Repeated dosing at 10 mg/kg/day resulted in little or no accumulation of [^{14}C-phenyl] foramsulfuron with the exception of the liver, where concentrations of [^{14}C-phenyl] foramsulfuron increased by 2.5–2.8× between day 1 (0.08/0.11 µg/g) and day 14 (0.22–0.28 µg/g) of dosing. Metabolism of [^{14}C-phenyl] foramsulfuron following single low- and high-dosing was similar between sexes and dose groups, with the parent compound being the major residue recovered in the feces (72.3–80.4% dose). The parent compound was also the major metabolite found in the feces of repeat-dose males (64.3%) and females (98.1%). Metabolites identified in the feces and urine included the cleavage product AE F153745 (1.6–11.0% dose) and the free amine metabolite AE F130619 (0.8–3.5% dose). Minor amounts of unknown metabolites were also detected in the feces (≤5.9% dose) and urine (≤3.9% dose).

Foramsulfuron technical has low acute toxicity by the oral, dermal and inhalation routes of exposure. It is non-irritating to the skin, minimally irritating to the eye and is not considered a potential skin sensitizer. The formulation Option 35 DF Herbicide has low acute toxicity by the oral, dermal and inhalation routes of exposure. It is moderately irritating to the skin, mildly irritating to the eye and is a potential skin sensitizer. The formulants are of no toxicological concern. The second formulation, Option 2.25 OD Liquid Herbicide, is considered to be of low acute toxicity by the oral, dermal and inhalation routes in rats. The formulation was minimally irritating to the rabbit eye and was moderately irritating to the rabbit skin. Results of skin sensitization testing in guinea pigs, based on Buehler's method, showed a positive response for skin sensitization.

In a 28-day dermal toxicity study in rats, foramsulfuron did not affect mortality, clinical signs, body weight, body-weight gain, food consumption, hematology, clinical chemistry, organ weight or gross pathology. At 1000 mg/kg bw/day, sebaceous hyperplasia at the application site and slight lymphocytic infiltration of the liver were observed in male rats only. The no observed adverse effect level (NOAEL) for systemic toxicity was 1000 mg/kg bw/day (limit dose).

In mice, decreased leukocytes, lymphocytes and monocytes were observed in the high-dose (6400 ppm) males in the 90-day study; however, these changes were not corroborated by other findings indicative of leukopenia, such as altered bone marrow histology or splenomegaly. No other effects on clinical signs, body weight, body weight gain, food consumption, haematology, gross- or histopathological findings were observed. The NOAEL for the 90-day dietary study was 6400 ppm (equivalent to 1002 and 1179 mg/kg bw/day in males and females, respectively), the highest dose tested. In the 78-week combined dietary/oncogenicity study, no treatment-related effects were noted and no increase in tumour incidence was observed. The NOAEL for the 78-week study was 8000 ppm (equivalent to 1115.1 and 1375.5 mg/kg bw/day in males and females, respectively), the highest dose tested. There was no evidence of carcinogenic potential of foramsulfuron in mice.

In rats, no treatment-related or adverse findings were noted in the 90-day dietary study or the two-year combined dietary/oncogenicity study. The NOAEL for the 90-day dietary study was 20 000 ppm (equivalent to 1568 and 1786 mg/kg bw/day in males and females, respectively), the highest dose tested. The NOAEL for the two-year study was 20 000 ppm (equivalent to 849 and 1135 mg/kg bw/day in males and females, respectively), the highest dose tested. There was no evidence of carcinogenic potential of foramsulfuron in rats.

Foramsulfuron was tested in a battery of in vitro (bacterial and mammalian cell gene mutation assays, unscheduled DNA synthesis assay and mammalian cell chromosomal aberration assay) and in vivo (mouse micronucleus assay) mutagenicity studies. Foramsulfuron showed weak clastogenic activity in primary human lymphocytes in the absence of exogenous metabolic activation. However, there was no evidence of genotoxic potential in any other assay. Therefore, the weight of evidence suggests that foramsulfuron was not genotoxic under the conditions of the tests performed.

Rat and rabbit developmental toxicity studies and a two-generation rat reproduction study indicated that foramsulfuron was not teratogenic or a reproductive toxicant. In the rat two-generation reproductive study, there were no treatment-related effects on parental systemic toxicity, reproductive function, reproductive parameters, litter parameters or offspring toxicity at dose levels up to and including 15 000 ppm (equivalent to 1082 and 1229 mg/kg bw/day in parental males and females, respectively, and to 1349 and 1434 mg/kg bw/day in F_1 parental males and females, respectively), the limit dose. The NOAEL for parental, offspring and reproductive toxicity was 15 000 ppm (equivalent to 1082 and 1229 mg/kg bw/day in parental generation males and females, respectively, and to 1349 and 1434 mg/kg bw/day in F_1 generation males and females, respectively). Based on the parental and offspring NOAELs, there was no indication that neonates were more sensitive to foramsulfuron exposure.

In the rat developmental study, there were no adverse treatment-related maternal or developmental findings at dose levels up to and including 1000 mg/kg bw/day, the limit dose. The NOAEL for maternal and developmental toxicity was 1000 mg/kg bw/day, and no lowest observed adverse effect level (LOAEL) was observed. In the rabbit developmental study, reddish urine was observed in a few dams during days 10–12 of gestation. However, there were no adverse treatment-related findings for any reproductive or developmental parameters at dose levels up to and including 500 mg/kg bw/day. The NOAEL for maternal and developmental toxicity was 500 mg/kg bw/day, and no LOAEL was observed. On the basis of the maternal and developmental NOAELs noted in the rat and rabbit developmental studies, there was no quantitative evidence to suggest an increased susceptibility of the fetus to in utero exposure to foramsulfuron.

3.2 Determination of Acceptable Daily Intake

The most appropriate NOAEL recommended for the acceptable daily intake (ADI) is 849 mg/kg bw/day (the highest dose tested) as determined in the two-year rat dietary study. A safety factor of 100× is recommended (10× for intraspecies variation, 10× for interspecies variation). No sensitivity was observed; therefore, the PCPA factor can be reduced to 1×. The recommended ADI is 8.49 mg/kg bw/day.

$$\text{ADI} = \frac{\text{NOAEL}}{\text{UF}} = \frac{849 \text{ mg/kg bw/d}}{100} = 8.49 \text{ mg/kg bw/day}$$

3.3 Determination of Acute Reference Dose

Refer to Regulatory Document REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*, for a detailed assessment of the determination of the acute reference dose of foramsulfuron and its end-use products.

3.4 Occupational and Bystander Risk Assessment

Refer to Regulatory Document REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide,* for a detailed assessment of the occupational and bystander risk assessment of foramsulfuron and its end-use products.

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 foramsulfuron. The data gathering and enforcement analytical methodology, HPLC-MS method, is valid for the quantification of foramsulfuron residues and the metabolite, AE F153745 (not a residue definition), in field corn grain, forage and stover. The residues of foramsulfuron are stable when stored in a freezer at –20°C for 866 days (corn grain), 617 days (corn forage) and 621 days (corn stover). Raw agricultural commodities (RACs), including corn grain, forage and stover, were processed into germ, grits, flour, meal, starch, grain dust and

refined oil. Estimation of concentration factors could not be obtained as no quantifiable residues were observed in the RACs. Supervised residue trials conducted throughout the United States and Canada using end-use products containing foramsulfuron in or on field corn are sufficient to support the proposed maximum residue limit (MRL). There is no expectation of secondary transfer of foramsulfuron residues from the treated crop to livestock feedstuffs. Therefore, MRLs for animal commodities are not required.

3.5.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 1.3), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following assumptions were made in a basic level chronic analysis: MRL value for corn commodities. The basic chronic dietary exposure from all supported foramsulfuron food uses (alone) for the total population is essentially 0% (i.e. 0.000013%) of the ADI. Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to foramsulfuron from food and water is essentially 0% (i.e. 0.000025%) of the ADI for the total population. The highest exposure is for all infants (<1 year) at 0.000056% of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

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

3.5.3 Aggregate Exposure and Risk

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

3.5.4 Maximum Residue Limits

A maximum residue limit of 0.01 ppm on field corn grain has previously been established in Table II, Division 15 of the Food and Drugs Regulations.

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 methodology, field trial data and chronic dietary risk estimates are summarized in Appendix I, Tables 3 and 4.

4.0 Impact on the Environment

Refer to Regulatory Document REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide,* for a detailed assessment of the environmental impact of foramsulfuron and its end-use products.

The previously outstanding information on the *n*-octanol–water partition coefficient for three major transformation products, one minor transformation product and Lemna toxicity studies with the end-use products, Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide, were submitted. A study for seedling emergence with end-use product Option 2.25 OD Liquid Herbicide was initially required. However, the study had previously been reviewed and reported as vegetative vigour. The submitted vegetative vigour study had not been reviewed, and thus was reviewed under these submissions. All data, except those for Option 2.25 OD Liquid Herbicide, were found acceptable. There is still an outstanding data requirement for Option 2.25 OD Liquid Herbicide toxicity to *Lemna* sp.

4.1 Fate and Behaviour in the Environment

There were concerns regarding the potential for three transformation products to bioaccumulate in organisms. The log K_{ow} was determined for three transformation products of foramsulfuron using the shake flask method and a fourth using the HPLC method. The log K_{ow} was predicted as follows: 2.14 (pH 3) for AE F130619; 0.92 for AE F092944; −2.2 (pH 4), −2.3 (pH 7) and −2.5 (pH 9) for AE 0338795; and −0.62 for AE F153745. Therefore, none of these transformation products are expected to bioaccumulate.

There were concerns regarding the stability of foramsulfuron and its major transformation products in the stored samples from the field dissipation studies. To address this concern, a storage stability study was submitted for foramsulfuron and the major transformation product, AE F092944, in soil obtained from the field study sites. For formasulfuron, the half-life was calculated to be 936 days under frozen conditions. The transformation product half-life was much shorter at 264 days, which is shorter than the storage period for samples in the field dissipation study. However, AE F092944 is not a residue of concern and is not expected to bioaccumulate; therefore, laboratory data are sufficient.

The fate and behaviour of foramsulfuron in the terrestrial and aquatic environments are summarized in Appendix I, Tables 5 and 6, respectively.

4.2 Environmental Risk

The risk assessment integrates the environmental exposure and ecotoxicity data to estimate the potential for adverse ecological effects. Since publication of Regulatory Note REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*, the PMRA has moved from margins of safety to levels of concern (LOC) based on the risk quotient (RQ). The RQ is the ratio of the expected environmental concentration (EEC) and toxicity endpoint chosen. The LOC for potential adverse effects on the test organism is considered to be an RQ of 1. For the screening level risk assessment, an RQ of <1 indicates that use of the product is expected to pose a negligible risk, and no further analysis is required. If the screening level risk assessment results in an RQ of ≥1, then the risk is further refined and/or it has to be mitigated.

Under the original review, EECs in water were calculated for 30 cm of water. Under the new aquatic risk scenario, the water body has been changed to 15 cm for amphibians and 80 cm for all other aquatic organisms. The resulting EECs for Option 2.25 OD Liquid Herbicide in water are 0.7 and 0.5 mg EP/L, respectively, and the corresponding values for Option 35 DF Herbicide are 0.067 and 0.013 mg EP/L. The other change has been the endpoints used to determine risk, which are documented in Appendix I, Tables 9 and 10. Only those studies reviewed or used to determine the new risk assessment are included in these tables.

Owing to issues with the original review, the vegetative vigour study submitted for Option 2.25 OD Liquid Herbicide was not originally reviewed. Additionally, there was some confusion and incorrect seedling emergence data were reported. Therefore, the vegetative vigour study was reviewed at that time and a new risk assessment on terrestrial vascular plants was conducted. Under the screening level risk assessment, RQ values based on the most sensitive endpoint were calculated to be 62.5 and 322.6 for Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide, respectively. Therefore, a refined Tier I risk assessment was conducted to further characterize the potential risk to non-target plants. Under this scenario, exposure to off-field (non-target) plants was refined using empirical spray drift curves to more accurately determine the amount of drift reaching plants one metre downwind from the edge of the application swath. Using a standard field sprayer with a boom height of 60 cm above the crop and an assumed American Society of Agricultural Engineers (ASAE) spray quality of “medium” for this herbicide application, only 6% of the on-target rate is expected to drift one metre downwind from the edge of the application site (based on data from Wolf and Caldwell, 2001). Therefore, the new EECs for Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide are 90 g EP/ha and 6 g EP/ha. However, this still results in risk to plant species, with calculated RQs of 3.8 and 19.4 for Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide, respectively. Therefore, buffer zones are required to reduce the risk of adverse effects on non-target plants.

Concerns regarding the risk of Option 35 DF Herbicide to aquatic vascular plants was addressed by the applicant. For Option 35 DF Herbicide, the toxicity was found to be 18 µg EP/L and the no observed effect concentration (NOEC) was 0.18 µg EP/L. This makes aquatic vascular plants the most sensitive aquatic species. The new methods for determining risk to aquatic organisms find that there is a risk of 13.9, which is greater than the LOC of 1. Therefore, buffer zones are required to mitigate this risk.

During the new aquatic risk assessment, the risk to amphibians was also determined. The LOC was found to be <1 for both Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide.

5.0 Value

5.1 Effectiveness Against Pests

Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide had been granted conditional registration with one of the conditions being that the lowest effective rate (LER) for lambsquarters, yellow foxtail, large crabgrass, barnyard grass and bristly foxtail be established. The registrant provided additional data to support the rate of 35 g a.i./ha for each of these weed species. The condition of conditional registration has now been adequately addressed from a value perspective and no further data are required.

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide

The submitted efficacy data established the LER for the Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide treatment applied alone and support the weed control and suppression claims that are summarized in Table 5.1 Option 35 DF Herbicide must be applied with Hasten spray additive at 1.0% v/v and 2.5 L/ha of 28% UAN. Option 2.25 OD Liquid Herbicide must be applied with 2.5 L/ha of 28% UAN.

Table 5.1 Weed Control and Suppression Claims for Option 35 DF Herbicide* and Option 2.25 OD Liquid Herbicide**

Herbicide Rate	Weeds Controlled	Weeds Suppressed
15 g a.i./ha or 43 g Option 35 DF Herbicide/ha 0.67 L Option 2.25 OD Liquid Herbicide/ha	Quackgrass, fall panicum, green foxtail, proso millet, witchgrass, common chickweed, wild mustard, wormseed mustard, eastern black nightshade, redroot pigweed, velvetleaf	
35 g a.i./ha or 100 g Option 35 DF Herbicide/ha 1.56 L Option 2.25 OD Liquid Herbicide/ha	All weeds above, in addition to barnyard grass, large crabgrass, yellow foxtail, bristly foxtail, lambsquarters	Common ragweed

* Option 35 DF Herbicide must be applied with Hasten spray adjuvant at 1.0% v/v and 2.5 L/ha of 28% UAN.
** Option 2.25 OD Liquid Herbicide must be applied with 2.5 L/ha of 28% UAN.

Refer to Regulatory Note REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide,* for a detailed assessment of the value and efficacy of Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide and a detailed assessment of the contribution to risk reduction and sustainability of Foramsulfuron Technical Herbicide.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, foramsulfuron was assessed in accordance with the Pest Management Regulatory Agency (PMRA) Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of foramsulfuron were also considered, including major transformation products formed in the environment, microcontaminants in the technical product and formulants in the end-use products, Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide. The PMRA has reached the following conclusions:

- Foramsulfuron does not meet the criteria for Track 1 substances.
- AE F130619 does not meet the criteria for Track 1 substances.
- AE F092944 does not meet the criteria for Track 1 substances.
- AE 0338795 does not meet the criteria for Track 1 substances.
- AE F153745 does not meet the criteria for Track 1 substances.
- Technical grade foramsulfuron does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.
- The end-use products Option 2.25 OD Liquid Herbicide and Option 35 DF Herbicide do not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

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

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for foramsulfuron is adequate to define the majority of toxic effects that may result from human exposure to foramsulfuron. In subchronic and chronic studies on laboratory animals, there were no effects on any organs. Chronic studies did not reveal any signs of cancer. Reproduction and developmental studies did not demonstrate maternal or fetal effects. The weight of evidence indicated that foramsulfuron was not genotoxic and it is not considered to be a neurotoxicant.

The nature of the residue in corn is adequately understood. The residue definition is foramsulfuron. The proposed use of foramsulfuron on field corn 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 an MRL to protect human health. An MRL of 0.01 ppm on field corn grain has previously been established in Table II, Division 15 of the Food and Drugs Regulations.

Refer to Regulatory Document REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*, for a detailed health risk assessment of foramsulfuron and its end-use products.

7.2 Environmental Risk

Formasulfuron end-use products present a risk to terrestrial and aquatic plants. Therefore, mitigative buffer zones have been added to the label. There is a general one-metre buffer zone for aquatic habitats, and a three-metre buffer zone for Option 2.25 OD Liquid Herbicide and a 10-metre buffer zone for Option 35 DF Herbicide for terrestrial habitats. The risk of Option 2.25 OD Liquid Herbicide to aquatic vascular plants is unknown. Thus, this end-use product is still under conditional registration due to outstanding information.

Refer to Regulatory Document REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide,* for a detailed environmental risk assessment of foramsulfuron and its end-use products.

7.3 Value

Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide had been granted conditional registration, one of the conditions being that the lowest effective rate for lambsquarters, yellow foxtail, large crabgrass, barnyard grass and bristly foxtail be established. The registrant provided additional data to support the rate of 35 g a.i./ha for each of these weed species. The condition of registration has now been adequately addressed from a value perspective and no further data are required.

There are two application rates for Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide. When applied at a rate of 15 g a.i./ha, these products will control quackgrass, fall

panicum, green foxtail, proso millet, witchgrass, common chickweed, wild mustard, wormseed mustard, eastern black nightshade, redroot pigweed and velvetleaf. When applied at 30 g a.i./ha, these products will control the listed weeds at 15 g a.i./ha plus barnyard grass, large crabgrass, yellow foxtail, bristly foxtail, lambsquarters, and will suppress common ragweed.

Refer to Regulatory Document REG2003-08, *Foramsulfuron Technical Herbicide, Option 2.25 SC Herbicide, and Option 35 DF Herbicide*, for a detailed value assessment of Option 35 DF Herbicide and Option 2.25 OD Liquid Herbicide.

8.0 Proposed Regulatory Decision

Health Canada's Pest Management Regulatory Agency, under the authority of the *Pest Control Products Act*, is proposing full registration for the sale and use of the technical grade active ingredient foramsulfuron and the end-use product Option 35 DF Herbicide to control certain broadleaf and grassy weeds in field corn. An evaluation of current scientific data from the applicant has resulted in the determination that, under the proposed conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

The risk posed by end-use product Option 2.25 OD Liquid Herbicide to aquatic plants is unknown. Option 2.25 OD Liquid Herbicide will remain a conditional registration until all of the additional information requirements have been addressed.

8.1 Additional Data Requirements

8.1.1 Data Requirements Related to Environmental Risks

The following additional information is required to refine the risk assessment.

A study determining the toxicity of Option 2.25 OD Liquid Herbicide to *Lemna* sp.

List of Abbreviations

µg	microgram(s)
a.i.	active ingredient
ADI	acceptable daily intake
bw	body weight
CAS	chemical abstracts service
cm	centimetre(s)
d	day(s)
DAT	days after treatment
DEEM	dietary exposure evaluation model
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time to 50% (the dose required to observe a 50% decline in the test population)
EC_{25}	effective concentration on 25% of the population
EEC	estimated environmental concentration
EP	end-use product
F	female
F_1	first generation offspring
FDA	*Food and Drugs Act*
g	gram(s)
GC	gas chromatography
h	hour(s)
ha	hectare(s)
HPLC	high performance liquid chromatography
kg	kilogram(s)
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LER	lowest effective rate
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOQ	limit of quantitation
m	metre(s)
M	male
mg	milligram(s)
mL	millilitre(s)
MMAD	mass median aerodynamic diameter
MRL	maximum residue limit
MS	mass spectrometry
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NZW	New Zealand white
PCPA	*Pest Control Products Act*

pH	-log 10 hydrogen ion concentration
PHI	preharvest interval
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RAC	raw agricultural commodity
RQ	risk quotient
SC	soluble concentrate
$t_{1/2}$	half-life
TRR	total radioactive residue
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
v/v	volume per volume dilution
yrs	years

Appendix I Tables

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Plant	EM F02/99-0	foramsulfuron and 4,6-dimethoxypyrimidin-2-amine	HPLC/UV	0.01 mg/kg in maize kernel	
Animal	EM F07/00-0	foramsulfuron	LC/MS/MS[1]	0.01 mg/kg in meat, fat and liver	
	FS-001-A05-01	foramsulfuron sulfonamide	LC/MS/MS[2]	50 µg/kg in chicken breast	1060305
Soil	CF/02/98	foramsulfuron	HPLC/UV	0.002 µg/kg	
		dimethoxypyrimidin-2-amine	GC/MS		
Sediment	FS-002-S05-01	foramsulfuron	LC/MS/MS[3]	2 µg/L	1060303
		foramsulfuron sulfonamide			
Water	EM/F07/99-00	foramsulfuron	HPLC/UV	0.1 µg/L in drinking and surface water	
	FS-003-W05-01	foramsulfuron and 4-amino-2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino] sulfonyl]-N,N-dimethylbenzamide	LC/MS/MS[4]		1060304

[1] Foramsulfuron transition: 453.2 to 182.0

[2] Foramsulfuron sulfonamide transition: 272 to 227

[3] Foramsulfuron transition: 451 to 296
Foramsulfuron sulfonamide transitions: 272 to 255

[4] Foramsulfuron transition: 451 to 296
4-amino-2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-N,N-dimethylbenzamide transition: 423 to 268

Table 2 Toxicology Summary Table

ACUTE STUDIES–Option 2.25 OD Liquid Herbicide			
Oral - rat	**AE F130360 + AE F122006, 22.5 + 22.5 g/L oil flowable**; Code AE F130360 01 1K05 A304; rat, SD, 5/sex, 5000 mg/kg bw	LD_{50}, ♂♀ > 5000 mg/kg bw	Mortality: 1/sex, within minute of dosing Clinical signs: piloerection, hunched posture, waddling/unsteady gait, lethargy, walking on toes and pallid extremities Less common signs: partially closed eyelids, thin/ungroomed appearance All surviving rats normal by day 9 Bw: all survivors gained weight Gross pathology: thickening of the stomach wall and gaseous distension of the duodenum **Low toxicity**
Dermal - rat (24 h exposure)	**AE F130360 + AE F122006, 22.5 + 22.5 g/L oil flowable**; Code AE F130360 01 1K05 A304; batch 945/990301 rat, SD, 5/sex, 5000 mg/kg bw	LD_{50}, ♂♀ > 5000 mg/kg bw	Mortality: nil Clinical signs: nil Bw: most gained weight; 3 ♀ had lower bw gains Skin irritation: slight to well-defined irritation reaction from day 2 with desquamation from day 4; normal by day 12 Gross pathology: nil **Low toxicity**
Inhalation - rat (4-h nose only)	**AE F130360 + AE F122006, 22.5 + 22.5 g/L oil flowable**; Code AE F130360 01 1K05 A304; batch KD945/990301 rat, SD, 5/sex, 5.25/77 mg/L (actual/nominal concentration)	LC_{50}, ♂♀ > 5.25 mg/L MMAD ± GSD = 4.64 µm ±2.15 <4 µm = 42.3% aerosol	Mortality: nil Clinical signs: During exposure - wet fur, irregular respiration Postexposure - wet fur, hunched posture, piloerection, ↑ respiratory rate, red/brown stain around snout Bw: normal gains Gross pathology: nil **Low toxicity**
Eye irritation - rabbit	**AE F130360 + AE F122006, 22.5 + 22.5 g/L oil flowable**; Code AE F130360 01 1K05 A304; batch KD945/990301 rabbit, NZW, 4♂, 0.1 mL not rinsed	Maximum mean score at 1 h = 12/110	Mortality: nil Clinical signs: nil Eye irritation: mean scores at hour 1 and days 1, 2, 3, 4 were 12, 5.33, 2.67, 1.33, 0, respectively Irritation index = 3.11/110 **Minimally irritating**

Skin irritation - rabbit	**AE F130360 + AE F122006, 22.5 + 22.5 g/L oil flowable**; Code AE F130360 01 1K05 A304; batch KD945/990301 rabbit, NZW, 3♂, 0.5 mL; not rinsed	Maximum mean score at day 4–5 = 5/8	Mortality: nil Clinical signs: nil Skin irritation: mean scores at days 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 were 3.67, 4.67, 4.33, 5, 5, 4, 4, 3.33, 2, 1.3, 0.33, 0, (maximum = 8), respectively Irritation index = 4.67/8 **Moderately irritating**
Dermal sensitization - guinea pig (Buehler's method)	**AE F130360 + AE F122006, 22.5 + 22.5 g/L oil flowable**; Code AE F130360 01 1K05 A304; batch KD945/990301 guinea pig, Dunkin/Hartley, ♀; 20 in test, 10 in negative control group	induction - 0.5 mL undiluted challenge - 0.5 mL of 25%, v/v, in sterile water	Adequate inductions Could even use lower concentrations Adequate controls Reaction after challenge: positive in 2/20 animals **Potential skin sensitizer**

Table 3 Integrated Food Residue Chemistry Summary

Nature of the Residue in Corn		Reference: 1021725
Radiolabel	phenyl	pyrimidyl
Test site	field	greenhouse
Treatment	foliar	foliar
Rate (1 application only)	60 g a.i./ha or 261 g a.i./ha	60 g a.i./ha or 240 g a.i./ha
End-use product	water dispersible granule	
Pre-harvest interval	77 days	106 days
Foramsulfuron is metabolized in corn via two routes. One route involves hydrolysis of the sulfonylurea bridge resulting in formation of AE F153745 and AE F092944. The other route involves hydrolysis of the formamide moiety of the phenyl ring, yielding AE F130619. The petitioner stated that these metabolites are then further degraded, yielding highly polar, water-soluble components.		
Major metabolites (>10% of the TRRs)	Foramsulfuron (AE F130360)	
Minor metabolites	AE F130619, AE F153745 and AE F092944	
Residue definition	Foramsulfuron	
Confined Rotational Crop Study - Soybeans, Radish and Wheat		Reference: 1021741
Formulation used for trial	Foramsulfuron, water dispersible granule	
Application rate and timing	62.2–65.6 g a.i./ha (twice the maximum proposed seasonal rate) applied once to bare soil, and crops planted at 119 days after treatment (DAT); 92.6–93.2 g a.i./ha (three times the maximum proposed seasonal rate) applied once to bare soil, and crops planted at 30, 59 and 269 DAT.	

Succeeding crops	Identified Metabolites
PH Label- wheat straw	None identified
PY Label - Soybean forage, wheat forage, wheat grain, wheat straw	None identified
Residue definition	Foramsulfuron

Nature of the Residue in Livestock	Reference: 1021726, 1021727		
Species	**Radiolabel**	**Dose Level**	**Sacrifice**
Cow (*British Friesian*)	[U-^{14}C phenyl-]Foramsulfuron; 12.87 µCi/mg	187.4 mg/kg bw/day for seven consecutive days. Equivalent to 15.99 ppm in the diet.	22 h after final administration
18.2% of total administered dose in edible tissues/organs and milk; 6.6% in urine; 75.2% in feces.			
Hen (*Warrens strain*)	[U-^{14}C phenyl-]Foramsulfuron; 996.2 µCi/mg	1.5 mg/bird/day for 14 consecutive days. Equivalent to 10 ppm in the diet.	22 h after final administration
6.6% of total administered dose in edible tissues/organs and eggs; 93.4% excreted.			

Major metabolites (>10% of the TRRs)	Cow	Hen
	Muscle, fat, kidney and milk: Foramsulfuron, AE F153745 Liver: Foramsulfuron	Egg yolk (10 days): Foramsulfuron Egg yolk (14 days): AE F153745 Liver: Foramsulfuron, AE F153745
Proposed metabolic pathway	Hen: Foramsulfuron is either rapidly cleared or poorly absorbed in poultry because systemic distribution to tissues is low. Much of the administered dose was eliminated as unchanged parent. Cow: Foramsulfuron was mainly excreted as unchanged compound. AE F153745 was the only identifiable cleavage product.	
Residue definition	Foramsulfuron	

Crop Field Trials—Corn	Reference: 1021738, 1021739

A total of 23 field trials were conducted over the 1997 to 1998 period in the American Zones 1 (2 trials), 2 (1 trial), 5 (18 trials), 6 (2 trials); and in Canada Zones 5 (2 trials) and 5B (4 trials). Treatments conducted at 2 to 3 times the maximum proposed seasonal rate.

Commodity	Total Application Rate, g a.i./ha	PHI (days)	Analyte	Residue Levels (ppm)		
				Min.	Max.	HAFT
Forage	80–94	37–67	Foramsulfuron	< 0.05	< 0.05	< 0.05
Grain	80–94	60–120	Foramsulfuron	< 0.01	< 0.01	< 0.01
Stover	80–94	65–151	Foramsulfuron	< 0.05	< 0.05	< 0.05
Forage	80–94	37–67	AE F153745	< 0.05	< 0.05	< 0.05

Grain	80–94	60–120	AE F153745	< 0.02	< 0.02	< 0.02
Stover	80–94	65–151	AE F153745	< 0.05	< 0.05	< 0.05

Field Accumulation in Rotational Crops - Soybeans, Wheat	Reference: 1021742
The application rate was 60 g a.i./ha for soybeans and 90 g a.i./ha for wheat. Residues of foramsulfuron and AE F153745 were reported. Wheat samples were collected but not analyzed. Residues of foramsulfuron and AE F153745 were below the method LOQ in soybean forage (<0.05 ppm for both metabolites), hay (<0.05 ppm for both metabolites) and seed (<0.01 ppm for foramsulfuron, <0.02 ppm for AE F153745).	
Processed Food and Feed	Reference: 1021740
Residues of foramsulfuron and AEF153745 were less than the method LOQ for corn forage (<0.05 ppm), stover (<0.05 ppm) and grain (<0.01 ppm for foramsulfuron, <0.02 ppm for AE F153745). Therefore, no further analyses of the processed commodities were conducted. No concentration factor considered for the petitioned uses.	
Storage Stability	Reference: 961890; 1021724
Residues of foramsulfuron and AE F153745 were stable at -20°C for up to approximately 28 months (866 days) in or on corn grain, up to 20 months (617 days) in or on forage and up to 20 months (621 days) in or on stover. The periods evaluated covered the interval between storage and analysis of the corn samples in the supervised trials.	
Livestock Feeding	Reference: Not applicable
Based on the lactating cow and poultry metabolism studies conducted at highly exaggerated rates compared to the maximum theoretical dietary burden, no finite residues of foramsulfuron equivalents are expected in the livestock tissues. A feeding study was therefore considered unnecessary at this time.	

Table 4 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT **Primary crops (corn)** **Rotational crops (soybean, radish, wheat)**	 Foramsulfuron Foramsulfuron
METABOLIC PROFILE IN DIVERSE CROPS	The profile in diverse crops cannot be determined because only corn was investigated.
ANIMAL STUDIES	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT AND RISK ASSESSMENT	Foramsulfuron
METABOLIC PROFILE IN ANIMALS (cow and hen)	Similar profiles were seen in the cow and hen.
FAT SOLUBLE RESIDUE	No

DIETARY RISK FROM FOOD AND WATER			
Refined chronic non-cancer dietary risk **ADI = 8.49 mg/kg bw** **Estimated chronic drinking water concentration = 0.53 µg a.i./L**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
	All infants <1 yr old	0	0
	Children 1 to 2 yrs	0	0
	Children 3 to 5 yrs	0	0
	Children 6 to 12 yrs	0	0
	Youth 13 to 19 yrs	0	0
	Adults 20 to 49 yrs	0	0
	Adults 50+ yrs	0	0
	Females 13 to 49 yrs	0	0
	Total population	0	0

Table 5 Fate and Behaviour in the Environment

Property	Test Substance	Value	Comments
Phototransformation on soil	foramsulfuron (AE F130360)	Not determined	Insufficient data, but not expected to be an important route.
Biotransformation in aerobic soil	foramsulfuron (AE F130360)	DT_{50}: 1.2–3.5 d (clay loam) DT_{50}: 6.6 d (loamy sand) DT_{50}: 8.7 d (silty clay loam) DT_{50}: 9.5 d (sandy loam)	AE F130619 and AE F092944 are major transformation products.
	AE F130619 (major transformation product)	DT_{50}: 0.2–0.3 d (loam) DT_{50}: 0.4 d (sand) DT_{50}: 0.8 d (sandy loam)	
Biotransformation in anaerobic soil	foramsulfuron (AE F130360)	DT_{50}: 229.8 d (sandy loam)	Foramsulfuron is persistent in sandy loam soil under anaerobic conditions.

Property	Test Substance	Value	Comments
Mobility			
Adsorption/desorption in soil	foramsulfuron (AE F130360)	Adsorption K_{oc} (mL/g): silty clay loam: 151 loamy sand: 51–89 clay: 63 sand: 38	In the soils tested, foramsulfuron had high to very high mobility.
	AE F153745 (major transformation product)	Adsorption K_{oc} (mL/g): sand: 63 sandy loam: 50 clay loam: 35 loam sediment: 48	In the soils and sediment tested, AE F153745 had high to very high mobility.
	AE F130619 (major transformation product)	Adsorption K_{oc} (mL/g): loam: 144 sandy loam: 63 sand: 44 clay loam: 40	In the soils tested, AE F130619 had high to very high mobility.
	AE F092944 (major transformation product)	Adsorption K_{oc} (mL/g): silt loam: 11 289 silty clay: 917 sandy loam: 395–696 loamy sand: 89–663 sand: 211	For most of the soils tested, AE F092944 had low to moderate mobility; however, the compound was immobile in silt loam and had high mobility in one loamy sand tested.
Field studies			
Field dissipation		DT_{50} for Ecoregion 8.1, Mixed Wood Plains (Ontario sites and New York): 11–18 d DT_{50} for Ecoregion 9.2, Temperate Prairies (Missouri): 13 d	Non-persistent to slightly persistent under field conditions.
Field leaching	No data	–	No data

Table 6 Fate and Behaviour in the Aquatic Environment

Property	Test Material	Value	Comments
Abiotic transformation			
Hydrolysis	foramsulfuron (AE F130360)	pH 4: 4.5 d pH 5: 10.6 d pH 7: 156 d pH 9: 176 d	Not a principal route of transformation.
	AE F130619 (major transformation product)	pH 7: 140 d	
Phototransformation in water	foramsulfuron (AE F130360)	77–106 d	Not a route of transformation.
Biotransformation			
Biotransformation in aerobic water/sediment systems	foramsulfuron (AE F130360)	First order half-lives (and DT_{50}s) <u>Total System</u> Silt clay loam: 31 d (DT_{50} = 34 d) Sand: 38 d (DT_{50} = 55 d) <u>Sediment</u> Silt clay loam: 43 d (DT_{50} = 55 d) Sand: 46 d (DT_{50} = 43 d)	Foramsulfuron is slightly persistent in aerobic water/sediment systems and slightly to moderately persistent in the sediment phase.
Biotransformation in anaerobic water/sediment systems	foramsulfuron (AE F130360)	First order half-lives (and DT_{50}s) <u>Total system</u> Silty clay loam: 39 d (DT_{50} = 31 d) <u>Sediment</u> Silty clay loam: 61 d (DT_{50} = 45d)	Foramsulfuron is slightly persistent in anaerobic water/sediment systems and slightly to moderately persistent in the sediment phase.
Field studies			
Field dissipation	Not applicable	–	No aquatic field study submitted.

Table 7 Toxicity to Non-Target Terrestrial Species

Organism	Exposure	Test Substance	Endpoint Value	Degree of Toxicity
Vascular plants				
Vascular plants	Seedling emergence	Option 2.25 OD Liquid Herbicide	EC_{25}: 77.7 g EP/ha (radish) NOEC: 30.6 g EP/ha (radish)	
		Option 35 DF Herbicide	EC_{25}: 25 g EP/ha (ryegrass) NOEC: 5.4 g EP/ha (tomato)	
	Vegetative vigour (shoot weight and height)	Option 2.25 OD Liquid Herbicide	EC_{25}: 24 g EP/ha (radish) NOEC: 11 g EP/ha (radish)	
		Option 35 DF Herbicide	EC_{25}: 0.29 g EP/ha (oat) NOEC: 0.17 g EP/ha (radish)	

Table 8 Toxicity to Non-Target Aquatic Species

Organism	Exposure	Test Substance	Endpoint Values
Vascular plants (*Lemna gibba*)	7-d acute	Foramsulfuron (98%)	EC_{50}: 0.00052 mg a.i./L NOEC: 0.00033 mg a.i./L
		AE F15375 (96%) (major transformation product)	EC_{50} > 100 mg TP/L NOEC = 100 mg TP/L
		Option 35 DF Herbicide	EC_{50}: 0.0018 mg EP/L NOEC: 0.00018 mg EP/L
		Option 2.25 OD Liquid Herbicide	Data gap

Table 9 Screening Level Risk Assessment on Non-Target Terrestrial Species

Organism	Exposure	Test Substance	Endpoint Value	EEC	RQ
Vascular plants					
Non-target terrestrial vascular plants	Seedling emergence	Option 2.25 OD Liquid Herbicide	EC_{25}: 77.7 g EP/ha	1500 g EP/ha	19.3
		Option 35 DF Herbicide	EC_{25}: 25 g EP/ha	100 g EP/ha	4
	Vegetative vigour	Option 2.25 OD Liquid Herbicide	EC_{25}: 24 g EP/ha	1500 g EP/ha	62.5
		Option 35 DF Herbicide	EC_{25}: 0.29 g EP/ha	100 g EP/ha	344.8

Table 10 Screening Level Risk Assessment on Non-Target Aquatic Species

Organism	Exposure	Test Substance	Endpoint Value	EEC	RQ
Aquatic vascular plants	Dissolved	foramsulfuron	NOEC: 0.00033 mg a.i./L	0.012 mg a.i./L	36.4
		AE F153745 (major transformation product)	EC_{50} > 100 mg TP/L	—	
		Option 2.25 OD Liquid Herbicide	data gap	0.19 mg EP/L	not calculated
		Option 35 DF Herbicide	½ EC_{50}: 0.0009 mg EP/L	0.013 mg/L	13.9

Table 11 Refined Risk Assessment on Non-Target Species

Organism	Exposure	Test Substance	Endpoint Value	EEC	RQ
Non-target terrestrial vascular plants	Seedling emergence	Option 2.25 OD Liquid Herbicide	EC_{25}: 77.7 g EP/ha	90 g EP/ha	1.2
		Option 35 DF Herbicide	EC_{25}: 25 g EP/ha	6 g EP/ha	0.24
	Vegetative vigour	Option 2.25 OD Liquid Herbicide	EC_{25}: 24 g EP/ha	90 g EP/ha	3.75
		Option 35 DF Herbicide	EC_{25}: 0.29 g EP/ha	6 g EP/ha	20.7

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

Maximum residue limits (MRLs) have been previously established in Table II, Division 15 of the Food and Drugs Regulations.

Table 1 Comparison Between Canadian MRLs, American Tolerances and Codex MRLs

Commodity	Canada (ppm)	United States (ppm)	Codex* (ppm)
Field corn grain	0.01	Exempted**	Not reviewed by Codex

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

** The pesticide foramsulfuron is exempted from the requirement of a tolerance in corn grain, corn forage and corn stover when applied as a herbicide in accordance with good agricultural practices.

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

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

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