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Proposed Registration Decision

Flucarbazone-sodium

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Overview

Proposed Registration Decision for Flucarbazone-sodium

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of technical grade active ingredient flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide to control wild oats, green foxtail and selected broadleaf weeds in spring wheat and durum wheat.

An evaluation of available scientific information found that, under the approved conditions of use, the end-use products have value and do not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 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 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 hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive human populations (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

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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."

Before making a final registration decision on flucarbazone-sodium, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Registration Decision on flucarbazone-sodium, 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 in this consultation document.

What is Flucarbazone-sodium?

Flucarbazone-sodium is the technical grade active ingredient in the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide, which are postemergence herbicides used to control wild oats, green foxtail and selected broadleaf weeds in spring wheat and durum wheat.

Health Considerations

Can Approved Uses of Flucarbazone-sodium Affect Human Health?

Flucarbazone-sodium is unlikely to affect your health when used according to label directions.

Potential exposure to flucarbazone-sodium may occur through the diet (food and water) or when handling and applying the products. 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 (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

The active ingredient Everest Technical Herbicide and the two end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide have low acute toxicity hazards. Flucarbazone did not cause cancer in animals and was not genotoxic. There was no indication that flucarbazone caused damage to the nervous system, nor did it affect reproduction. There was also no indication that the fetus was more sensitive than the adult animal to flucarbazone. Toxicity following repeated dosing at very high doses included stomach and liver effects, decreased body weight, increased or decreased food consumption and discoloured feces. Some sporadic evidence of immunotoxicity was revealed during the standard testing regime. However, a directed and thorough

immunotoxicity study revealed no effects. The risk assessment was conducted to ensure that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Aggregate dietary intake estimates (food plus water) revealed that the general population and infants, the population group that would ingest the most flucarbazone-sodium 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 flucarbazone-sodium is not of concern for all population groups. The results of the cancer studies were negative; therefore, a chronic cancer dietary risk assessment was not required.

Animal studies revealed no acute health effects. Therefore, an acute dietary risk assessment was 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 Canada and the United States using flucarbazone-sodium on wheat were acceptable. The MRLs for this active ingredient can be found in the Science Evaluation of this consultation document.

Occupational Risks From Handling Flucarbazone-sodium

Occupational risks are not of concern when flucarbazone-sodium is used according to label directions, which include protective measures.

Farmers and pesticide applicators mixing, loading or applying Everest 70 WDG Herbicide or Everest Solupak 70 DF Herbicide and field workers entering freshly treated fields can come in direct contact with flucarbazone-sodium on the skin. For this reason, the label specifies that anyone mixing or loading Everest 70 WDG Herbicide or Everest Solupak 70 DF Herbicide must wear a long-sleeved shirt, long pants and chemical-resistant gloves. Taking into consideration these protective measures and the fact that occupational exposure is expected to be limited to one application per year, risk to farmers, applicators and workers is not a concern.

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

Environmental Considerations

What Happens When Flucarbazone-sodium Is Introduced Into the Environment?

Flucarbazone-sodium is slightly persistent in soils under field conditions. Aerobic biotransformation of flucarbazone in soil is a principal route of transformation in the terrestrial environment. The major transformation products detected in soils were sulfonamide, sulfonic acid, *O*-desmethyl MKH 6562 and *N*-methyltriazolinone. The parent compound and transformation products have a low potential to leach and contaminate groundwater under field conditions.

Flucarbazone-sodium is persistent and moderately persistent in water under aerobic and anaerobic conditions, respectively. Sulfonamide, *N*-methyltriazolinone and *N,O*-dimethyl triazolinone were the major transformation products detected in water. Low values of vapour pressure and Henry's law constant indicate that flucarbazone-sodium is essentially non-volatile and no significant volatilization is expected. Flucarbazone-sodium has a negligible potential for bioconcentration/bioaccumulation in organisms.

The active ingredient, flucarbazone-sodium, is relatively non-toxic to honey bees and earthworms. It is also practically non-toxic to bobwhite quail on an acute basis and slightly toxic on a dietary basis. It is detrimental to reproductive performance of mallard ducks, but is non-toxic to rats on an acute basis and on a dietary basis up to 250 mg a.i./kg diet. On an acute basis, flucarbazone-sodium is practically non-toxic to fish and other aquatic invertebrates but is toxic to freshwater algae. Flucarbazone-sodium is also very phytotoxic to non-target terrestrial and aquatic plants.

The parent compound, flucarbazone-sodium, and its transformation products do not meet the Toxic Substances Management Policy (TSMP) criteria for Track 1 substances. Flucarbazone-sodium does not contain any byproducts or microcontaminants that meet the TSMP Track 1 criteria.

Conversion from temporary to full registration does not result in unacceptable risks to the environment. Environmental concerns are mitigated with the existing label.

Value Considerations

What is the Value of Everest 70 WDG and Everest Solupak 70 DF Herbicides?

A single application of Everest 70 WDG Herbicide or Everest Solupak 70 DF Herbicide, hereafter referred to as Everest, provides effective control of wild oats, green foxtail and selected broadleaf weeds in spring wheat and durum wheat. Everest is compatible with integrated weed management practices and with conventional crop production systems. Given that Everest is applied after weeds have emerged, farmers can better assess whether the herbicide is necessary or suitable for particular weed species.

These Everest herbicides were granted conditional registration with one of the conditions being to provide additional efficacy data to support an application rate of 21.5 g/L Everest (15 g a.i./ha flucarbazone-sodium) for the control of green foxtail in spring wheat and durum wheat. The registrant has submitted adequate data to support the claim of green foxtail control at an application rate of 15 g a.i./ha flucarbazone-sodium and the conditional registration requirement has now been adequately addressed from a value perspective. 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.

The key risk-reduction measures being proposed for the labels of flucarbazone-sodium, Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Given that there is a concern with users coming into direct skin contact with flucarbazone-sodium, anyone mixing or loading Everest 70 WDG Herbicide or Everest Solupak 70 DF Herbicide must wear a long-sleeved shirt, long pants and chemical-resistant gloves, and anyone applying the product must wear a long-sleeved shirt and long pants.

Label recommendations
All three labels currently recommend vomiting and/or the use of syrup of ipecac. The PMRA has published new labelling guidance under Regulatory Directive DIR2007-01, *First Aid Labelling Statements.* Please update labels to reflect this guidance.

If the applicant wishes to retain the previous recommendations (as they appear on the draft label), please confirm with an emergency medicine professional on the appropriateness of the use of syrup of ipecac and inducing vomiting in the event that these products are swallowed.

Next Steps

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

Other Information

At the time the PMRA makes its registration decision, it will publish a Registration Decision on flucarbazone-sodium (based on the Science Evaluation in this consultation document and Regulatory Note REG2000-09, *Flucarbazone-sodium*). 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

Flucarbazone-sodium

1.0 The Active Ingredient, Its Properties and Uses

A detailed assessment of the chemical properties of flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide are presented in Regulatory Note REG2000-09, *Flucarbazone-sodium*.

1.1 Directions for Use

Flucarbazone-sodium is present in two end-use products, Everest 70 WDG Herbicide, formulated as a water dispersible granule, and Everest Solupak 70 DF Herbicide, formulated as a water dispersible granule in water soluble packets, which have a guarantee of flucarbazone (present as flucarbazone-sodium) at 66%.

Everest 70 WDG or Everest Solupak 70 DF Herbicides, hereafter referred to as Everest, is a selective herbicide for use as a postemergent application to spring wheat and durum wheat grown in Manitoba, Saskatchewan, Alberta and the Peace River Region of British Columbia to control wild oats, green foxtail and selected broadleaf weeds (Table 1.1.1). Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v (i.e. 0.25 L surfactant/100 L spray solution) with a maximum of one application per year using ground equipment only.

Table 1.1.1 Weed Control Claims on the Everest* Labels

Treatment	Weeds Controlled in Spring Wheat and Durum Wheat
Everest* (as a stand-alone treatment)	
15 g a.i./ha	Green foxtail
20 g a.i./ha	Wild oats, green foxtail, redroot pigweed, wild mustard, stinkweed, volunteer canola and green smartweed

Treatment		Weeds Controlled in Spring Wheat and Durum Wheat
Tank-Mix Partners with 15 g a.i./ha Everest*		
For use in spring wheat only	**For use in durum wheat only**	
2,4-D amine or ester Buctril M Estaprop Dichlorprop-D Refine Extra + 2,4-D amine	2,4-D amine or ester	Green foxtail plus weeds listed on the tank-mix partner label
Tank-Mix Partners with 30 g a.i./ha Everest*		
For use in spring wheat only	**For use in durum wheat only**	
2,4-D amine or ester Ally + 2,4-D amine or ester Attain Herbicide Tank Mix Buctril M Curtail M Dyvel Dyvel DS Estaprop Dichlorprop-D Express pack Frontline 2,4-D Herbicide Tank-Mix Frontline Tank-Mix MCPA amine or ester Pardner Prestige Herbicide Tank-Mix Refine Extra + 2,4-D amine or ester Target Spectrum Herbicide Tank-Mix Thumper Unity Herbicide Tank Mix	2,4-D amine or ester Frontline Tank-Mix Spectrum Herbicide Tank-Mix	Wild oats, green foxtail plus weeds listed on the tank-mix partner label

* Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v.

The following crops may be planted 11 months after an application of Everest (Table 1.1.2).

Table 1.1.2 Rotational Crops May Be Planted 11 Months After Application of Everest

Soil Zones and Rotational Crops			
Gray-Wooded	**Black**	**Dark Brown**	**Brown**
Spring wheat Barley Canola Field peas	Spring wheat Durum wheat Barley Canola Field peas Flax Field beans	Spring wheat Durum wheat Barley Canola Field peas Flax	Spring wheat

1.2 Mode of Action

Everest is a Group 2 herbicide (inhibitor of the enzyme acetolactate synthase, also known as acetohydroxy acid synthase), which catalyzes the first reaction in the biosynthetic sequence leading to the branched chain amino acids valine, leucine and isoleucine. Within a few hours, this inhibited synthesis of the branched chain amino acids leads to a secondary inhibition of DNA synthesis and a rapid cessation of plant growth. In the field, seedlings of sensitive weeds stop growth, occasionally turn red because of stress anthocyanins synthesis, wither, then eventually die back.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

Two solvent-programmed reverse phase high-performance liquid chromatographic methods were used to determine the active ingredients and five significant structurally related impurities (content $\geq$ 0.1%) in the technical product. The methods have been shown to have satisfactory specificity, linearity, precision and accuracy.

2.2 Methods for Residue Analysis

Refer to Regulatory Document REG2000-09, *Flucarbazone-sodium*, for a detailed assessment of the data-gathering and enforcement analytical method for plant commodities, the data-gathering method for animal commodities, and the multi-residue method for flucarbazone-sodium.

A new liquid chromatography with tandem mass spectrometry (LC-MS/MS) method that determines residues of flucarbazone-sodium in ruminant tissues and milk was submitted to replace the original enforcement method for animal matrices. This new method measures flucarbazone-sodium directly, rather than converting flucarbazone-sodium-related residues to flucarbazone-sodium sulfonamides via a common moiety method. The limit of quantitation

(LOQ) was 0.01 ppm for tissues, and 0.0025 ppm for milk. Milk and tissue samples were spiked at the LOQ and at five times the LOQ. The proposed data-gathering/enforcement method was adequately validated in bovine tissues and milk, with individual recoveries ranging from 73–105% over all matrices and spiking levels. A successful independent laboratory validation was completed with goat kidney and milk, indicating good reproducibility and reliability. Satisfactory extraction efficiency data were submitted for goat kidney and milk . No interference testing or confirmatory method was proposed as the detector used was highly specific. Therefore, the method was deemed acceptable for enforcement purposes in ruminant matrices.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Refer to REG2000-09 for a detailed assessment of the toxicological database for flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide.

3.2 Occupational and Residential Risk Assessment

Refer to REG2000-09 for a detailed assessment of the occupational risk for flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide.

3.3 Food Residues Exposure Assessment

Refer to REG2000-09 for a detailed assessment of the food residue database for flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide.

Confined Rotational Crops
The confined crop rotation study indicated that residues of flucarbazone-sodium and the sulfonamide conjugates were shown to be stable in phenyl-labelled samples of wheat forage for 629 days, wheat straw for 583 days and turnip roots for 238 days. However, the storage stability of flucarbazone-sodium residues in phenyl-labelled samples of turnip tops and kale for 238 days (7.8 months) was not addressed. In response, an addendum to the confined rotational crop study was submitted, demonstrating that flucarbazone-sodium residues in wheat (forage, straw, hay, grain), kale and turnip (top, root) samples are stable for 69 months.

Freezer Storage Stability
The freezer storage stability study indicated that residues of flucarbazone-sodium and *N*-desmethyl flucarbazone were stable in wheat forage, wheat hay and wheat straw for 25 months when stored at –20°C. In wheat grain, however, only the *N*-desmethyl flucarbazone was shown to be stable over the 25-month storage period. In response, a separate storage stability study was submitted, demonstrating that flucarbazone-sodium residues in wheat grain and mustard greens were stable for 49 months, which covers the storage periods in the wheat metabolism and supervised residue trial studies.

Livestock Feeding
According to the supervised residue trials conducted in representative growing locations in North America, residues of flucarbazone-sodium and *N*-desmethyl flucarbazone are unlikely to exceed 0.27, 0.08 and 0.04 ppm, respectively, in the livestock feed items, forage, hay and straw when treated according to the Canadian use pattern. On the basis of the maximum anticipated theoretical dietary burdens of flucarbazone-sodium and *N*-desmethyl flucarbazone to dairy cattle, residues in meat (including meat byproducts, excluding liver), liver and milk are expected to be 0.01 ppm or less, 0.05 ppm or less, and 0.005 ppm or less (based on the LOQ of the common moiety method), respectively, when flucarbazone-sodium is used according to label directions.

On the basis of the maximum anticipated theoretical dietary burdens of flucarbazone-sodium and the metabolic profile in poultry, no quantifiable residues of flucarbazone-sodium or any compound of toxicological interest in poultry meat and eggs are expected.

An MRL of 0.05 ppm is recommended to cover residues of flucarbazone-sodium in both ruminant and hog liver, based on the presence of quantifiable residues. The MRLs for all other animal commodities are to be set at the new method LOQs of 0.01 ppm (ruminant and hog meat, ruminant and hog meat byproducts except liver, poultry meat, poultry meat byproducts and eggs) and 0.0025 ppm (milk).

Dietary Risk Assessment
Refer to REG2000-09 for a detailed assessment of the dietary risk assessment.

The use of flucarbazone-sodium (Everest 70 WDG and Everest Solupak 70DF) on wheat grown in Canada does not pose an unacceptable chronic dietary (both food and water) risk to any segment of the population, including infants, children, adults and seniors.

The integrated food residue chemistry is summarized in Appendix I, Table 2.

3.3.1 Proposed Maximum Residue Limits

Table 3.3.1 Proposed Maximum Residue Limits

MRLs (ppm)	Foods
0.05	Liver of cattle, goats, hogs, horses and sheep
0.01	Meat and meat byproducts of cattle, goats, hogs, horses, poultry and sheep; eggs
0.0025	Milk

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

The nature of the residues in animal and plant matrices, analytical methodology, field trial data, and acute and chronic dietary risk estimates are summarized in Appendix I, Tables 1, 2 and 3.

4.0 Impact on the Environment

Refer to REG2000-09 for a detailed environmental assessment of flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide.

5.0 Value

5.1 Effectiveness Against Pests

Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide were granted conditional registration with one of the conditions being that additional efficacy data be provided to support an application rate of 21.5 g/L Everest (15 g a.i./ha flucarbazone-sodium) for the control of green foxtail in spring wheat and durum wheat. The registrant has submitted adequate data to support the claim of green foxtail control at an application rate of 15 g a.i./ha flucarbazone-sodium. Therefore, the condition of registration has now been adequately addressed from a value perspective and no further data are required.

Data were generated from 18 small-plot field trials conducted over a three-year period at several locations in Manitoba and Saskatchewan. For each trial, an appropriate experimental design was used, and an appropriate set of treatments was included to address the pest claim.

5.1.1 Acceptable Efficacy Claims

5.1.1.1 Everest Applied as a Stand-Alone Herbicide Treatment

The submitted efficacy data established the lowest effective rate (LER) for the Everest treatment applied alone. The data support the weed control claims that are summarized in Table 5.1.1. Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v.

Table 5.1.1 Weed Control Claims for Everest* as a Stand-Alone Treatment

Herbicide Rate	Weeds Controlled
15 g a.i./ha (21.5 g product/ha)	Green foxtail
20 g a.i./ha (28.5 g product/ha)	Above weed plus wild oats, redroot pigweed, wild mustard, stinkweed, volunteer canola, green smartweed

* Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v.

5.1.1.2 Herbicide Tank-Mix Combinations

The submitted efficacy data established an application rate for the Everest component of the tank-mix combinations. The data support the weed control claims summarized in Table 5.1.2. Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v.

Table 5.1.2 Weed Control Claims for the Everest* Component of the Herbicide Tank-Mix Combination

Application Rate for the Everest Component of the Tank-Mix Combinations	Weeds Controlled
15 g a.i./ha (21.5 g product/ha)	Green foxtail
30 g a.i./ha (43 g product/ha)	Above weed plus wild oats

* Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v.

5.2 Phytotoxicity to Host Plants

Crop tolerance data were generated from 185 small-plot field trials that tested spring wheat and durum wheat over a four-year period at sites in Manitoba, Saskatchewan and Alberta.

Crop injury was visually assessed up to three times during the growing season and was expressed as percentage injury. Crop yield, expressed as a percentage of a weedy or weed-free check, was also reported for the maximum application rate (1× rate) and the 2× rate.

5.2.1 Acceptable Claims for Host Plants

Crop injury data on Everest support a crop tolerance claim for spring wheat and durum wheat when viewed in conjunction with the crop yield data.

5.3 Impact on Succeeding Crops

It has previously been established that Everest may safely be applied as a postemergent herbicide to spring wheat and durum wheat to selectively control green foxtail, wild oats and selected broadleaf weeds. Recropping data were required to establish that the proposed rotational crops may safely be planted in soil previously treated with Everest.

All trials were conducted as randomized complete design experiments with either three or four replicates with visual assessments of crop injury. They were performed up to three times during the growing season, and yield was reported.

A recropping interval of 11 months was proposed for seven crops (spring wheat, durum wheat, barley, canola, field peas, field beans and flax) following an application of Everest (Table 1.1.2).

Based on the information made available, acceptable crop injury and yield were reported for spring wheat (15 trials), durum wheat (11 trials), barley (15 trials), canola (14 trials), field peas (11 trials), field beans (7 trials) and flax (8 trials). As such, these crops may appear on the product label as rotational crops to be planted 11 months following an application of Everest.

5.3.1 Acceptable Claims for Rotational Crops

The submitted crop injury and yield data support a rotational crop tolerance for spring wheat, durum wheat, barley, canola, field peas, field beans and flax planted 11 months following application of Everest.

5.4 Economics

Over 12 million hectares of spring and durum wheat are grown in the western provinces of Canada. From this, over 30 million tonnes of wheat are harvested with over 70% being sold as export to countries all over the world. Canada's position as the "bread basket of the world" is dependent upon a reliable supply of high quality wheat. Canada's ability to provide this has led to its ranking as the premium supplier of this crop in the world. Many former importing wheat countries such as India and Russia are now becoming exporters as they seek ways to attract foreign currency through trade. Canadian wheat growers must be able to compete with these new competitors who often sell for prices far below their actual production cost. Growers trying to stay competitive have aimed to increase wheat yields while reducing input costs.

5.5 Sustainability

5.5.1 Survey of Alternatives

Nonchemical means of weed control include cultivation and crop rotation. The postemergent use of Everest in spring wheat and durum wheat would not exclude the use of cultivation. Recropping data indicates that numerous crops may be planted 11 months following application of Everest.

Application of Everest would not exclude the sequential use of other herbicides with different modes of action for control of annual and perennial weeds not controlled by the product alone.

There are numerous postemergent herbicides, with different modes of action, that may be used alone or in various tank-mix combinations to control green foxtail and wild oats in spring wheat and durum wheat. Alternative active ingredients include, but are not limited to, clodinafop-propargyl (Group 1), fenoxaprop-p-ethyl (Group 1), tralkoxydim (Group 1), diclofop-methyl (Group 1 and 6), imazamethabenz (Group 2), propanil (Group 7), difenzoquat (Group 8) and flamprop-methyl (Group 25). They are now commercially available.

5.5.2 Compatibility With Current Management Practices Including Integrated Pest Management

Everest will provide control of green foxtail, wild oats and selected broadleaf weeds in spring wheat and durum wheat at a low rate of active ingredient per hectare.

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

The management of pesticide resistance development is an important part of sustainable and integrated pest management programs. Everest offers a unique perspective to the current integrated pest management programs and would assist in the long-term management of weeds at levels below those causing economic injury. The majority of available herbicides for use on spring and durum wheat to control green foxtail and wild oats have the same mode of action (inhibitors of acetyl CoA carboxylase or ACCase) and are classified as Group 1 herbicides.

Everest offers a different mode of action than the leading grassy weed control products. Everest is a Group 2 herbicide that controls green foxtail and wild oats by inhibiting acetolactate synthesis, also called acetohydroxy acid synthesis. Everest will contribute to risk reduction by playing a significant role in the rotation of herbicide groups, thereby reducing the risk of weed resistance.

Repeated use of herbicides with the same mode of action in a weed control program increases the probability of naturally selecting the biotypes, a group of plants within a species with biological traits that are not common to the population as a whole. There is also less susceptibility to the herbicides using that mode of action.

The Everest herbicide label includes the resistance management statements found in Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

6.0 Toxic Substances Management Policy Considerations

Refer to REG2000-09 for a detailed evaluation of TSMP considerations for flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide.

7.0 Summary

7.1 Human Health and Safety

Mixers, loaders, applicators and workers entering treated corn fields are not expected to be exposed to levels of flucarbazone-sodium that will result in unacceptable risk when the Everest 70 WDG Herbicide or Everest Solupak 70 DF Herbicide is used according to label directions. The personal protective equipment on the product label is adequate to protect workers and no additional personal protective equipment is required.

The nature of the residue in wheat plants and animals is adequately understood. The residue definition for enforcement and risk assessment purposes is flucarbazone-sodium for plant and animal matrices. The use of flucarbazone-sodium on wheat does not pose an unacceptable chronic dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified under the authority of the *Pest Control Products Act*.

Residues of flucarbazone-sodium in and on the following:

- milk (0.0025 ppm)
- wheat grain (0.01 ppm)
- egg (0.01 ppm)
- meat of cattle, goats, hogs, horses, poultry and sheep (0.01 ppm)
- meat byproducts of cattle, goats, hogs, horses, poultry and sheep (0.01 ppm)
- liver of cattle, goats, hogs, horses and sheep (0.05 ppm)

7.2 Environmental Risk

Conversion from temporary to full registration did not result in any increased risks to the environment as the environmental exposure was not increased. Therefore, additional environmental data were not required to support this conversion. Environmental concerns were mitigated on the existing label.

7.3 Value

Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide are selective herbicides for use as a postemergent application to spring wheat and durum wheat grown in Manitoba, Saskatchewan, Alberta and the Peace River Region of British Columbia to control wild oats, green foxtail and selected broadleaf weeds. Everest must be applied with a non-ionic surfactant such as Agral 90 or Ag-Surf at an application rate of 0.25% v/v (i.e. 0.25 L surfactant/100 L spray solution) with a maximum of one application per year using ground equipment only.

The registrant has submitted adequate data to support the claim of green foxtail control, and the condition of registration has now been adequately addressed from a value perspective. No further data are required. When applied as a stand-alone treatment, Everest controls green foxtail at an application rate of 15 g a.i./ha. When applied as a stand-alone treatment, Everest controls green foxtail, wild oats and selected broadleaf weeds at an application rate of 20 g a.i./ha.

When applied in a tank-mix combination, Everest controls green foxtail at an application rate of 15 g a.i./ha. When applied in a tank-mix combination, Everest controls green foxtail and wild oats at an application rate of 30 g a.i./ha.

Spring wheat, durum wheat, barley, canola, field peas, field beans and flax may be planted 11 months following an application of Everest.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act*, is proposing full registration for the sale and use of the technical grade active ingredient flucarbazone-sodium and the end-use products Everest 70 WDG Herbicide and Everest Solupak 70 DF Herbicide to control wild oats, green foxtail and selected broadleaf weeds in spring wheat and durum wheat. An evaluation of current scientific data has resulted in the determination that, under the proposed conditions of use, the end-use products have value and do not present an unacceptable risk to human health or the environment.

List of Abbreviations

µg	microgram(s)
a.i.	active ingredient
ADI	acceptable daily intake
bw	body weight
DNA	deoxyribonucleic acid
DF	water dispersible granular herbicide in water soluble packets
g	gram(s)
ha	hectare(s)
ILV	interlaboratory validation
kg	kilogram(s)
L	litre(s)
LC-MS/MS	liquid chromatography with tandem mass spectrometry
LOD	level of detection
LOQ	limit of quantitation
mg	milligram(s)
MRL	maximum residue limit
PMRA	Pest Management Regulatory Agency
ppm	parts per million
TSMP	Toxic Substances Management Policy
v/v	volume per volume dilution
WDG	water dispersible granular herbicide

Appendix I Tables and Figures

Table 1 Residue Analysis

Methods for residue analysis of animal matrices	PMRA #
The revised residue definition for plant and animal matrices is flucarbazone-sodium. Analytical methods previously reviewed in REG2000-09 encompass this revised residue definition.	
Confirmatory method LC-MS/MS acts both as a method to detect and as a confirmatory method to quantitate the analytes of interest. An additional confirmatory method was not necessary. **Enforcement method** LC/MS/MS. LOQ = 0.01 ppm for tissues, 0.0025 ppm for milk. LOD = 0.0008-0.0033 ppm for milk, kidney, liver, fat and muscle. Acceptable recoveries from 73-105% in bovine milk and tissues. Satisfactory extraction efficiency data submitted for goat kidney and milk. **ILV** ILV indicated good reliability and reproducibility.	1070402 1070406 1070403

Table 2 Integrated Food Residue Chemistry Summary

Freezer storage stability tests
Study 1: Stability of flucarbazone-sodium + *N*-desmethyl flucarbazone residues in wheat forage, hay, straw and grain at –20°C for 34, 33, 28 and 24 months, respectively.
Plant metabolism and residue samples were stored within the time periods studied.
Study 2: Stability of flucarbazone-sodium and *N*-desmethyl flucarbazone residues in wheat grain and mustard seeds at 1511 days (48 months) of frozen storage at –15°C.

Study 1: [triazolinone-UL-^{14}C] flucarbazone-sodium label, TRRs (ppm) **PMRA #1070405**

Commodity	Flucarbazone-sodium residues			*N*-desmethyl flucarbazone residues		
	Initial residue level (ppm)	Initial residues recovered (%)	Stored sample residues recovered (%)	Initial residue level (ppm)	Initial residues recovered (%)	Stored sample residues recovered (%)
Wheat forage	0.480	100	96	0.75	92	95
Wheat hay	0.471	94	74	1.501	71	80
Wheat straw	0.237	76	72	0.558	72	90
Wheat grain	-	-	-	0.003	100	90

Study 2: [phenyl-UL-^{14}C] flucarbazone-sodium label, TRRs (ppm) **PMRA #1070404**

Commodity	Flucarbazone-sodium residues			*N*-desmethyl flucarbazone residues		
	Recovered residues (ppm)	Average recovery (%)	Overall decline (%)	Recovered residues (ppm)	Average recovery (%)	Overall decline (%)
Wheat grain	0.15–0.27	70–86	0	0.14–0.27	65–90	0
Mustard greens	0.24–0.30	86–97	11	0.21–0.27	79–91	12

Proposed MRLs

Commodity	Proposed Canadian MRLs (ppm)
Wheat grain	0.01
Meat of cattle, goats, hogs, horses, poultry and sheep	0.01
Meat byproducts of cattle, goats, hogs, horses, poultry and sheep	0.01
Liver of cattle, goats, hogs, horses and sheep	0.05
Milk	0.0025
Eggs	0.01

Table 3 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES		
RESIDUE DEFINITION FOR ENFORCEMENT Wheat		Flucarbazone-sodium
METABOLIC PROFILE IN DIVERSE CROPS		The profile in diverse crops cannot be determined because only wheat was investigated.
ANIMAL STUDIES		
ANIMALS		**Ruminant and poultry**
RESIDUE DEFINITION FOR ENFORCEMENT		Flucarbazone-sodium
METABOLIC PROFILE IN ANIMALS (goat, hen, rat)		The rat, goat and hen metabolism studies indicated that the major route of metabolism of flucarbazone-sodium was via hydrolysis to N,O-dimethyl triazolinone and to the flucarbazone sulfonamide metabolite, which appeared to conjugate to proteins in the liver. The minor metabolic routes differ slightly between the animals (rat, poultry and goat). However, all metabolites observed in the goat and poultry have been identified or accounted for in the rat metabolism.
FAT SOLUBLE RESIDUE		No
DIETARY RISK FROM FOOD AND WATER		
Refined chronic non-cancer dietary risk **ADI = 0.36mg/kg bw** **Estimated chronic drinking water concentration = 7.1 µg/L**	**POPULATION**	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**
		Food and Water
	All infants <1 year	0.2
	Children 1–6 years	0.1
	Children 7–12 years	0.1
	Females 13–19 years	0.1
	Females 20+ years	0.1
	Males 13–19 years	0.1
	Males 20+ years	0.1
	Seniors 55+ years	0.1
	Total population	0.1

	POPULATION	ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)	
		Food Only	Food and Water
	None. No endpoint of concern attributable to a single dose was identified.		

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

Eleven of the specified Canadian MRLs are the same as those in the United States. In nine cases, the MRL differs from the tolerance established in the United States (http://ecfr.gpoaccess.gov/cgi/t/text/text-idx?c=ecfr&sid=c413e0e915a0a6a80c50beb1efbaf09b&tpl=/ecfrbrowse/Title40/40cfr180_main_02.tpl) and Codex (www.codexalimentarius.net/mrls/pestdes/jsp/pest_q-e.jsp)

Table 1 Differences Between MRLs in Canada and Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Milk	0.0025	0.005	Not reviewed by Codex
Cattle, liver	0.05	1.50	
Goat, liver	0.05	1.50	
Horse, liver	0.05	1.50	
Sheep, liver	0.05	1.50	
Hog, liver	0.05	1.50	
Poultry, meat	0.01	None	
Poultry, meat byproducts	0.01	None	
Egg	0.01	None	

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

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For 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 discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

1.0 Methods of Analysis

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2.0 Value

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