Proposed Registration Decision PRD2010-24

Pyrasulfotole

(publié aussi en français)

23 September 2010

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario
K1A 0K9

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

Canada

HC Pub: xxxx

ISBN: 978-1-100-16872-2 (978-1-100-16873-9)
Catalogue number: H113-9/2010-24E (H113-9/2010-24E-PDF)

Table of Contents

Overview

Proposed Registration Decision for Pyrasulfotole

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 Pyrasulfotole Technical Herbicide, AE 0317309 02 SE06 Herbicide and Infinity Herbicide containing the technical grade active ingredient pyrasulfotole to control a range of broadleaf weeds in wheat (spring, durum and winter), barley, oats, triticale, and timothy (grown for seed production).

Pyrasulfotole Technical Herbicide (Registration Number 28737), AE 0317309 02 SE06 Herbicide (Registration Number 28736) and Infinity Herbicide (Registration Number 28738) are conditionally registered in Canada. The detailed review for pyrasulfotole, AE 0317309 02 SE06 Herbicide and Infinity Herbicide can be found in *ERC2007-11 - Pyrasulfotole*. The current applications were submitted to convert Pyrasulfotole Technical Herbicide, AE 0317309 02 SE06 Herbicide and Infinity Herbicide from conditional registration to full registration.

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

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Pyrasulfotole Technical Herbicide, AE 0317309 02 SE06 Herbicide and Infinity 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.

---

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."

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 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 section of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on pyrasulfotole, 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[4] on pyrasulfotole, 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 Pyrasulfotole?

Pyrasulfotole is a postemergence herbicide, i.e. a herbicide applied after the crop has emerged above the ground. It belongs to the chemical class of pyrazolones and is a pigment inhibitor or bleacher. Pyrasulfotole inhibits an enzyme in susceptible plants, which in turn disrupts the synthesis of essential pigments found in the leaves of all plants.

AE 0317309 02 SE 06 Herbicide contains the active ingredient pyrasulfotole only, while Infinity Herbicide is a coformulation of the active ingredients pyrasulfotole and bromoxynil.

Health Considerations

Can Approved Uses of Pyrasulfotole Affect Human Health?

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

People could be exposed to pyrasulfotole through diet (food and water) or when handling and applying the product. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (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.

[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*.

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 using pyrasulfotole products according to the label directions.

Pyrasulfotole end-use products AE 0317309 02 SE 06 Herbicide and Infinity Herbicide caused eye and skin irritation in rabbits. Infinity Herbicide was moderately acutely toxic when tested in rats.

When tested in laboratory animals, technical pyrasulfotole was not genotoxic[5], but at very high dose levels, induced urinary bladder tumours in male and female mice and a very low incidence of eye tumours in male rats. A 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.

At high dose levels, pyrasulfotole retarded the development of rat and rabbit fetuses. However, it did not affect reproductive performance in the rat. The rabbit teratology data demonstrated higher sensitivity of offspring when compared to the maternal animals. Studies did not provide evidence of teratogenicity in rats and rabbits or neurotoxicity in rats. There was no indication that pyrasulfotole affects the immune and endocrine systems.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that the general population and children, the subpopulation which would ingest the most pyrasulfotole relative to body weight, are expected to be exposed to less than 59.7% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from pyrasulfotole is not of concern for all population sub-groups.

A single dose of pyrasulfotole is not likely to cause acute health effects in the general population (including infants and children). An aggregate (food and water) dietary intake estimate for females 13-49 used less than 3.8% of the acute reference dose, which is not a health concern.

The Food and Drugs Act prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *The 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.

[5] Genotoxic chemicals are those capable of causing damage to DNA. Such damage can potentially lead to the formation of a malignant tumor, but DNA damage does not lead inevitably to the creation of cancerous cells.

Residue trials conducted throughout Canada and the United States using products containing pyrasulfotole on wheat, barley, oat, triticale and timothy (grown for seed production only) were acceptable. The MRLs for this active ingredient are listed on the Maximum Residue Limits for Pesticides webpage in the Pesticides and Pest Management section of Health Canada's website.

Occupational Risks From Handling AE 0317309 02 SE06 Herbicide and Infinity Herbicide

Occupational risks are not of concern when AE 0317309 02 SE06 Herbicide and Infinity Herbicide are used according to the proposed label directions, which include protective measures.

Farmers and custom applicators mixing, loading or applying AE 0317309 02 SE06 Herbicide or Infinity Herbicide as well as field workers re-entering freshly treated fields can come in direct contact with AE 0317309 02 SE06 Herbicide or Infinity Herbicide or through inhalation of spray mist. Therefore, the labels specify that a long-sleeved shirt, long pants, shoes and socks must be worn during application as well as chemical-resistant gloves and goggles or face shield must be worn during mixing/loading, clean-up and repair activities for both end-use products. The AE 0317309 02 SE06 Herbicide label requires that workers do not enter treated fields for 12 hours after application and the Infinity Herbicide label requires that workers do not enter treated fields for 24 hours. Taking into consideration these label statements, the number of applications and the expectation of the exposure period for handlers and workers, risks to these individuals are not a concern.

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

Environmental Considerations

What Happens When Pyrasulfoltole Is Introduced Into the Environment?

Pyrasulfotole enters the environment when used as a herbicide on cereal crops. Pyrasulfotole is moderately persistent in soil, mobile in soil, and persistent in water. The major breakdown product AE B197555 (pyrasulfotole-benzoic acid) is moderately persistent in soil, and was only found in minor amounts in water. Pyrasulfotole and AE B197555 are expected to leach through the soil profile beyond 30 cm; therefore they may be expected to enter groundwater. In surface waters, pyrasulfotole will partition to sediments and may be expected to accumulate in aquatic systems. Canadian field studies demonstrated that up to approximately 19% of applied pyrasulfotole is expected to carry over to the following growing season. Based on its low volatility, pyrasulfotole residues are not expected in the air.

Pyrasulfotole 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, given that pyrasulfotole is a herbicide, it is expected to adversely affect terrestrial plants in adjacent areas. Therefore, buffer zones of 2 to 375 metres (depending on end use product formulation and application equipment) are required to protect nearby plants from the effects of spray drift. The end-use product Infinity Herbicide also requires a 10 m aquatic buffer zone due to risk from bromoxynil in the formulation.

Value Considerations

What Is the Value of Pyrasulfotole?

Pyrasulfotole is a postemergence herbicide, i.e. a herbicide applied after the crop has emerged above the ground, to control lamb's quarters, redroot pigweed, wild buckwheat and volunteer canola (including herbicide tolerant varieties) in wheat (spring, durum and winter), barley, tame oats, triticale and timothy (grown for seed production).

A single application of pyrasulfotole provides effective control of lamb's quarters, redroot pigweed, wild buckwheat as well as volunteer canola in wheat (spring, durum and winter), barley, oats, triticale and timothy (grown for seed production). Pyrasulfotole is compatible with integrated weed management practices, conservation tillage, and conventional crop production systems. Pyrasulfotole is applied after weed emergence; therefore, growers are able to assess whether the herbicide is suitable for the particular weed species present. Pyrasulfotole also provides control of both conventional and herbicide tolerant canola types including glyphosate, glufosinate-ammonium and acetolactate synthase (ALS) tolerant canola types.

Measures to Minimize Risk

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

The key risk-reduction measures being proposed on the labels of AE 0317309 02 SE06 Herbicide and Infinity Herbicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with users coming into direct contact with AE 0317309 02 SE06 Herbicide and Infinity Herbicide via the skin, or through inhalation of spray mists, a long-sleeved shirt, long pants, shoes and socks must be worn during application. In addition, chemical resistant gloves and goggles or face shield must be worn during mixing/loading, clean-up and repair activities. Standard label statements to protect against drift during application were added to the label.

Environment

No new risk-reduction measures are required for the environment as a result of the new data submitted for the full registration of pyrasulfotole and its associated end-use products. Refer to ERC2007-11 for a full list of environmental risk-reduction measures required on product labels.

Next Steps

Before making a final registration decision on pyrasulfotole, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

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

Science Evaluation

Pyrasulfoltole

1.0 The Active Ingredient, Its Properties and Uses

Please refer to the Evaluation Report ERC2007-11 for details of the chemistry assessment.

1.1 Identity of the Active Ingredient

Purity of the active ingredient	97.8% nominal (limits 95-100%)

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

Technical Product—Pyrasulfotole Technical Herbicide

Property	Result
Density	1.53 g/mL (at 20°C)

End-Use Products— AE 0317309 02 SE06 Herbicide and Infinity Herbicide (AE 0317309 03 EC23 Herbicide)

New specifications for one of the formulants present in each of the two end-use products were provided.

1.3 Directions for Use

1.3.1 AE 0317309 02 SE06 Herbicide

AE 0317309 02 SE06 Herbicide is a selective herbicide for use as a post-emergence treatment on wheat (spring, durum and winter), barley, tame oats, triticale, and timothy (grown for seed production), for the control of lamb's quarters, redroot pigweed, wild buckwheat and volunteer canola (including herbicide tolerant varieties). The product is applied once per growing season at a rate of 50 g a.i./ha as a broadcast treatment with either ground or aerial application equipment.

1.3.2 Infinity Herbicide

Infinity Herbicide is a selective herbicide for use as a post-emergence treatment on wheat (spring, durum and winter), barley, triticale, and timothy (grown for seed production), for the control of a wide range of broadleaved weeds. The product is to be applied once per growing season at a rate of 205.5 g a.i./ha (31.125 g a.i./ha pyrasulfotole and 174.3 g a.i./ha bromoxynil) (Table 1.3.2.1) as a broadcast treatment with either ground or aerial application equipment.

Table 1.3.2.1 – Use pattern for Infinity Herbicide

Herbicide rate	Weeds Controlled	Weeds Suppressed
205.5 g a.i./ha or 0.83 L product/ha (174.3 g/ha bromoxynil + 31.125 g/ha pyrasulfotole)	annual sow-thistle, chickweed, cleavers, flixweed, hemp-nettle, kochia, lamb's-quarters, pale smartweed, redroot pigweed, Russian thistle, shepherd's-purse, stinkweed, volunteer canola (includes conventional and herbicide tolerant), wild buckwheat, wild mustard, common ragweed	Canada thistle, dandelion, perennial sow-thistle, round-leaved mallow

1.4 Mode of Action

Pyrasulfotole is classified as a Group 27 herbicide (refer to Regulatory Directive *DIR99-06, Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*). The primary mode of action of pyrasulfotole is as an inhibitor of the enzyme 4-hydroxyphenylpyruvate dioxygenase (4-HPPD) in susceptible plants, thereby disrupting the synthesis of carotenoids that are produced by plants to protect against oxidative and photolytic damage. Visible effects may not be observed for several days and appear as white splotches on the leaves of susceptible plants, as pyrasulfotole is a pigment inhibiting or bleaching herbicide.

2.0 Methods of Analysis

Please refer to ERC2007-11 for details on the methods of analysis.

2.1 Methods for Residue Analysis of Food and Animal Origin - Ruminant

Refer to ERC2007-11 for a summary of the data previously reviewed and the rationale for the regulatory decision.

An enforcement method that quantifies the parent pyrasulfotole and the metabolite pyrasulfotole-desmethyl in animal matrices was submitted and deemed to be acceptable. A high performance liquid chromatography-electrospray ionization with tandem mass spectrometry (LC-MS/MS) method was developed for the analysis of pyrasulfotole and the metabolite pyrasulfotole-desmethyl in ruminant matrices. The method fulfilled the requirements with regards to specificity, accuracy and precision at the respective method limits of quantitation. The limit of quantitation of 0.01 ppm for each analyte was demonstrated for bovine meat, kidney, liver and

fat, and the limit of quantitation of 0.005 ppm for each analyte was demonstrated for whole milk, skim milk and cream. Acceptable recoveries (70-120%) of pyrasulfotole and pyrasulfotole-desmethyl residues were obtained in ruminant matrices.

All data requirements pertaining to food residue exposure identified in the ERC2007-11 were adequately addressed by the applicant.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

Please refer to ERC2007-11 for details of the toxicology assessment.

3.2 Occupational and Residential Risk Assessment

Please refer to ERC2007-11 for details of the occupational exposure and risk assessment.

3.2.1 Occupational Exposure and Risk

To support the initial registration of pyrasulfotole, a full risk assessment was conducted for AE 0317309 02 SE06 Herbicide on wheat, barley, oats, timothy and triticale and for Infinity Herbicide on wheat, barley, timothy and triticale. Risk estimates for handlers and workers entering treated fields were found to be acceptable. Refer to ERC2007-11 for details.

3.2.2 Residential Exposure and Risk Assessment

3.2.3 Bystander Exposure and Risk

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

3.3 Food Residues Exposure Assessment

Please refer to ERC2007-11 for details of the residue exposure assessment.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Refer to ERC2007-11 for details of the environmental fate assessment.

The registrant has provided an additional study on the octanol/water partition coefficient (Log K_{ow}) for the pyrasulfotole transformation product AE B197555 (PMRA 1784084). The mean log K_{ow} values for octanol/water, octanol/ pH 4.4 buffer and octanol/ pH 8.1 buffers were -0.21, -1.0 and -2.0, respectively. Therefore, the pyrasulfotole transformation product AE B197555 (referred as RPA 203328 in PMRA 1326887) is not expected to readily partition to organic matter in the aquatic environment, regardless of pH.

4.2 Environmental Risk Characterization

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

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

Please refer to ERC2007-11 for details of the risk to terrestrial organisms.

4.2.2 Risks to Aquatic Organisms

Please refer to ERC2007-11 for details of the risk to aquatic organisms.

As a condition of registration, the registrant provided an additional chronic toxicity study to the sediment-dwelling freshwater midge *Chironomus riparius*. Exposure to pyrasulfotole in spiked sediments resulted in significant reductions in adult emergence of chironomid larvae. The most sensitive endpoint was emergence rate, with a 28-day NOEC of 115 mg a.i./kg dw (in sediment), or 31.7 mg a.i/L (in overlying water), based on mean measured test concentrations. No significant reductions in larval development rates were observed. The 28-day EC_{50} based on emergence rate and development rate effects were both greater than the highest test concentration (i.e., >464 mg a.i./kg dw [sediment], or >119.7 mg a.i/L [overlying water]).

4.2.3 Incident Reports

No environmental incident reports for pyrasulfotole have been provided to the PMRA. Two environmentally-related incident reports for products containing co-formulations with bromoxynil (the co-formulant in Infinity Herbicide) have been submitted. In both cases, the incident reports cite phytotoxic damage to non-target herbaceous plants.

5.0 Value

Please refer to ERC 2007-11 for details of the value assessment.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

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

Refer to ERC2007-11 for a full description of the TSMP considerations for pyrasulfotole.

During the review process, the pyrasulfotole transformation product AEB197555 was assessed in accordance with the PMRA Regulatory Directive DIR99-03[6] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- The pyrasulfotole transformation product AEB 197555 does not meet Track 1 criteria, and is not considered a Track 1 substance as it is not expected to bioaccumulate in aquatic organisms (log K_{ow} values at environmentally relevant pH levels range from -2.0 to -0.21).

[6] DIR99-03, The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[7].

The list is used as described in the PMRA Notice of Intent NOI2005-01[8] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[9], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade pyrasulfotole 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 product AE 0317309 02 SE06 Herbicide does 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*. However, it contains a petroleum distillate, which is a List 2 formulant. Therefore, the label for the end-use product AE 0317309 02 SE06 Herbicide will include the statement: "This product contains aromatic petroleum distillates that are toxic to aquatic organisms."

- The end-use product Infinity Herbicide does 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*. However, it contains a petroleum distillate, which is a List 2 formulant. Therefore, the label for the end-use product Infinity Herbicide will include the statement: "This product contains aromatic petroleum distillates that are toxic to aquatic organisms."

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02[10].

---

7 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette,* Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

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

9 DIR2006-02, PMRA Formulants Policy.

10 DIR2006-02, PMRA Formulants Policy.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for pyrasulfotole is adequate to define the majority of toxic effects that may result from human exposure to pyrasulfotole. In short- and long-term toxicity studies on laboratory animals, target organs included the eye, kidneys, urinary bladder, thyroid, and pancreas. At dose levels that were considered excessive, there was evidence of carcinogenicity based on an increased incidence of urinary bladder tumours in mice and eye tumours in male rats. There was evidence of increased susceptibility of the offspring in the rabbit teratology study.

Mixer, loader and applicators handling AE 0317309 02 SE06 Herbicide or Infinity Herbicide and workers re-entering treated cereal fields are not expected to be exposed to levels of AE 0317309 02 SE06 Herbicide or Infinity Herbicide that will result in an unacceptable risk when these products are used according to label directions. The personal protective equipment on the product labels is adequate to protect workers.

The nature of the residue in plants and ruminants is adequately understood. The residue definition for risk and enforcement purposes is pyrasulfotole and pyrasulfotole-desmethyl in plant and animal commodities. The proposed use of pyrasulfotole on timothy, wheat, barley, oats, rye and triticale does not constitute an unacceptable chronic or acute 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. A complete list of all pesticide MRLs established in Canada can be found on the Maximum Residue Limits for Pesticides webpage in the Pesticides and Pest Management section of Health Canada's website.

7.2 Environmental Risk

Pyrasulfotole and its major transformation product AE B197555 are of low risk to pelagic aquatic organisms at the maximum Canadian use rate of 50 g a.i./ha (maximum RQ of 0.45 for pyrasulfotole exposure to the floating macrophyte Lemna gibba). However, the risk to benthic organisms was not assessed as no toxicity studies with benthic organisms were provided by the registrant. Given pyrasulfotole's ability to partition to sediments, and its persistence in aquatic systems, pyrasulfotole accumulation in sediments is likely to result in exposure to sediment-dwelling organisms.

Pyrasulfotole does pose a risk to non-target dicot plants, however, this may be mitigated by the observance of buffer zones for sensitive terrestrial habitats. The difference in aerial buffer zones between the two end-use products (i.e., up to 85 metres for AE 0317309 02 SE06 Herbicide versus 375 metres for Infinity Herbicide) is due to the higher toxicity seen with the Infinity formulation which also contains the active ingredient bromoxynil. The bromoxynil content in Infinity Herbicide also poses a risk to freshwater organisms and therefore a 10 metres buffer zone is required for Infinity Herbicide when sprayed upwind of sensitive freshwater habitats.

Of primary concern is pyrasulfotole's potential for persistence and mobility in the environment. Pyrasulfotole is transformed to AE B197555, a low risk transformation product, and mineralized to CO_2 through microbial activity in aerobic soil. Transformation is initially rapid. However, it soon slows down, leaving significant residues in the soil which persist for longer than one year. In terrestrial field studies in Canadian locations (or equivalent US Ecozones), up to 19% of applied pyrasulfotole remained in soils at the beginning of the following growing season. Laboratory studies showed that a significant portion of the applied pyrasulfotole may physically bind to the soil matrix (i.e., 35 – 62% bound residues), however, the field studies also showed that it has the potential to move vertically in the soil column up to 1 m, which suggests that it can reach groundwater.

Once it reaches the aquatic environment, pyrasulfotole is expected to be persistent. It does not undergo hydrolysis or photolysis and was shown to be stable in aerobic and anaerobic water sediment systems. In aerobic surface waters, pyrasulfotole may partition to sediments, particularly if water / soil pH is <5, however, it is not readily transformed and therefore is not lost from the system. Ground water modelling with LEACHM and surface water modelling with PRZM/EXAMS predicts that concentrations will continue to accumulate in water bodies with no outflow. Predicted annual concentrations in groundwater (38 µg a.i./L) and closed prairie dugouts (> 53 µg a.i./L) after a 50 year modelling scenario are greater than the EEC used to predict risk to aquatic organisms in this review (i.e., 6.3 µg a.i./L in an 80 cm deep water body). Therefore, it is possible that continuous use of this pesticide at the same site for an extended number of years could result in surface water concentrations in closed systems that may pose a risk to some aquatic plants.

The data supplied indicate that sediment-dwelling aquatic invertebrates are not at long-term risk from pyrasulfotole exposure, and that the pyrasulfotole transformation product AE B197555 is not expected to bioaccumulate in the tissues of aquatic organisms. Therefore, these data do not alter the original environmental risk profile for pyrasulfotole, or its primary transformation product AE B197555.

7.3 Value

The data submitted to register AE 0317309 02 SE 06 Herbicide are adequate to describe its efficacy for use in wheat (spring, durum and winter), barley, tame oats, triticale, and timothy (grown for seed production). A single post-emergence application of AE 0317309 02 SE 06 Herbicide provides control of wild buckwheat and volunteer canola (including herbicide tolerant varieties), as well as lamb's quarters and redroot pigweed, in wheat (spring, durum, winter), barley, tame oats, triticale, and timothy (grown for seed production). The submitted phytotoxicity and yield data demonstrate an adequate margin of safety of labelled host crops to AE 0317309 02 SE 06 Herbicide. AE 0317309 02 SE 06 Herbicide (Group 27) provides an alternative mode of action to commonly used Group 2 and Group 4 herbicides.

The data submitted to register Infinity Herbicide are adequate to describe its efficacy for use in wheat (spring, durum and winter), barley, triticale, and timothy (grown for seed production). A single post-emergence application of Infinity Herbicide provides control of wild buckwheat and volunteer canola (including herbicide tolerant varieties) as well as lamb's quarters and redroot pigweed, in wheat (spring, durum, winter), barley, triticale, and timothy (grown for seed production). The submitted phytotoxicity and yield data demonstrate an adequate margin of safety of labelled host crops to Infinity Herbicide. Infinity Herbicide (Group 27) provides an alternative mode of action to commonly used Group 2 and Group 4 herbicides.

8.0 Proposed Regulatory Decision

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 Pyrasulfotole Technical Herbicide, AE 0317309 02 SE06 Herbicide and Infinity Herbicide containing the technical grade active ingredient pyrasulfotole to control a range of broadleaf weeds in wheat (spring, durum and winter), barley, oats, triticale, and timothy (grown for seed production).

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

List of Abbreviations

µg	micrograms
a.i.	active ingredient
ALS	acetolactate synthase
cm	centimetres
FDA	Food and Drugs Act
g	gram
ha	hectare(s)
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LOC	Level of Concern
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LC-MS/MS	liquid chromatography with tandem mass spectrometry
mg	milligram
mL	millilitre
MRL	maximum residue limit
NOEC	no observed effect concentration
PCPA	Pest Control Products Act
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RQ	risk quotient
TSMP	Toxic Substances Management Policy

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference
Beef Matrices	AI-006-A08-01	Pyrasulfotole, Pyrasulfotole-desmethyl	LC-MS/MS	0.01 ppm for each analyte in bovine muscle, liver, kidney and fat; 0.005 ppm for each analyte in bovine milk (whole, skim and cream)	1786262 1786263

Table 2 Toxicity to Non-Target Species

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]	PMRA#
Aquatic Invertebrates					
Chironomus riparius	Chronic, 28-day spiked sediment	Pyrasulfotole	NOEC = 31.7 mg a.i./L in overlying water Effects: emergence rate (most sensitive parameter)	n/a	1784085

[a] US EPA classification, where applicable

Table 3 Screening Level Risk Assessment on Non-Target Species

Organism	Test Substance	Exposure	End point value	EEC	RQ[a]
Chironomus riparius	Pyrasulfotole	Chronic, 28-day spiked sediment	NOEC = 31.7 mg a.i./L in overlying water	0.0063 mg a.i./L	0.0002

[a] Risk quotient = exposure / toxicity. Bold RQ values indicate that the risk quotient exceeds the PMRA LOC of 1.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number 1641652
Reference 2008, Pyrasulfotole Technical Herbicide, 08090DC, DACO: 2.1,2.11.1,2.11.2, 2.11.3,2.12,2.12.1,2.12.2,2.2,2.3,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9 CBI

PMRA Document Number 1641653
Reference 2008, Description of Materials Used to Produce the Product and Manufacturing Process of Pyrasulfotole Technical Material Produced by [CBI REMOVED], M-305463-01-1, DACO: 2.11.1, 2.11.2,2.11.3,2.11.4 CBI

PMRA Document Number 1641655
Reference 2008, Material accountability of pyrasulfotole (AE 0317309) technical material manufactured by [CBI REMOVED] Analytical profile of five production batches, M-303205-01-1, DACO: 2.12.1,2.13.1,2.13.2,2.13.3 CBI

PMRA Document Number 1641656
Reference 2008, Determination of [CBI REMOVED] of AE 0317309 (Pyrasulfotole), M-303799-01-1, DACO: 2.13.1,2.13.2 CBI

PMRA Document Number 1703257
Reference 2008, Analytical Method: Determination of [CBI REMOVED] in AE 0317309 (Pyrasulfotole) by photometry, LM-ICL-0168-CD048, DACO: 2.13.1 CBI

PMRA Document Number 1703258
Reference 2008, Validation of Analytical Method LM-ICL-0168-CD48: Determination of [CBI REMOVED] in AE 0317309 (Pyrasulfotole) by Photometry, VB-2008-06, DACO: 2.13.1 CBI

PMRA Document Number 1857414
Reference 2010, Cover Letter (Clarification Response), DACO: 0.8

PMRA Document Number 1857418
Reference 2007, Material accountability of [CBI REMOVED] manufactured at [CBI REMOVED] - Analytical profile of production batches, DACO: 2.13.3 CBI

PMRA Document Number 1857431
Reference 2010, Cover Letter (Clarification Response), DACO: 0.8

A. List of Studies/Information Submitted by Registrant

2.0 Human and Animal Health

PMRA Document Number 1786262
Reference 2009, Validation of Bayer CropScience Method AI-006-A08-02 An analytical method for the determination of residues of Pyrasulfotole and Desmethyl Pyrasulfotole in animal tissues and milk using LC/MS/MS, DACO: 7.2.2

PMRA Document Number 1786263
Reference 2009, Independent laboratory validation of Bayer Method AI-006-A08-02, An analytical method for the determination of residues of Pyrasulfotole and Desmethyl Pyrasulfotole in animal tissues and milk using LC/MS/MS, DACO: 7.2.3

2.0 Environment

PMRA Document Number 1784084
Reference 1994. RPA 202248, RPA 203328 and RPA 205834 Octanol/water partition coefficients. Rhone-Poulenc Secteur Agro Centre de Recherche de la Dargoire. Study No. 94-69. Doc. No. R&D/CRLD/AN/9416433. PMRA DACO 8.5

PMRA Document Number 1784085
Reference 2008. *Chironomus riparius* 28-day chronic toxicity test with Pyrasulfotole (tech.) in a water-sediment system using spiked sediment. Bayer CropScience AG Development-Ecotoxicology. Report ID EBAIP013. PMRA DACO 9.3.4

B. Additional Information Considered

i) Unpublished Information

3.0 Environment

PMRA Document Number 1614025
Reference 2008. Incident Report for Mextrol 40 Liquid Herbicide (Reg. #26999). pp 7.

PMRA Document Number 1808665
Reference 2009. Incident Report for Benchmark A (Reg. #28787) and Benchmark B (Reg. #28876). pp 5.