Proposed Re-evaluation Decision PRVD2011-04

Fenoxaprop-P-ethyl

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide fenoxaprop-P-ethyl, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the Pest Control Products Act and Regulations, is proposing continued registration of products containing fenoxaprop-P-ethyl for sale and use in Canada.

An evaluation of available scientific information found that products containing fenoxaprop-P-ethyl do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of fenoxaprop-P-ethyl uses, new risk-reduction measures must be included on the labels of all products. Additional data are also being requested as a result of this re-evaluation.

This proposal affects all end-use products containing fenoxaprop-P-ethyl registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for fenoxaprop-P-ethyl and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of fenoxaprop-P-ethyl.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

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

Fenoxaprop-P-ethyl, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (for example, the federal Toxic Substances Management Policy [TSMP]).

The PMRA conducted a human health risk assessment for fenoxaprop-P-ethyl. A recent environmental risk assessment of fenoxaprop-P-ethyl from the European Union (EU) was found to be an adequate basis for the proposed Canadian re-evaluation decision.

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

What Is Fenoxaprop-P-ethyl?

Fenoxaprop-P-ethyl is a herbicide that is used to control certain annual and perennial grass weeds in cereals, certain pulse crops, vegetables, certain feed and forage crops, as well as ryegrass grown for seeds, and turfgrass. Fenoxaprop-P-ethyl is applied using aerial or ground application equipment.

Health Considerations

Can Approved Uses of Fenoxaprop-P-ethyl Affect Human Health?

Fenoxaprop-P-ethyl is unlikely to affect your health when used according to the revised label directions.

People could be exposed to fenoxaprop-P-ethyl by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Maximum Residue Limits

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 *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue at the established MRL does not pose an unacceptable health risk.

Fenoxaprop-P-ethyl is currently registered in Canada for use on cereals, certain pulse crops, vegetables, certain feed and forage crops and could be used in other countries on crops that are imported into Canada. No specific MRLs have been established for fenoxaprop-P-ethyl in Canada. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL will be implemented in the future, as indicated in the December 2009 Information Note, *Progress on Minimizing Reliance on the 0.1 Parts per Million as a General Maximum Residue Limit for Food Pesticide Residue*.

Environmental Considerations

What Happens When Fenoxaprop-P-ethyl Is Introduced Into the Environment?

Fenoxaprop-P-ethyl is unlikely to affect non-target organisms when used according to the revised label directions.

Birds, mammals, aquatic organisms, insects, other non-target arthropods, non-target terrestrial plants and soil non-target micro-organisms could be exposed to fenoxaprop-P-ethyl in the environment. Environmental risk is assessed by using the toxicity exposure ratio method - the ratio of the predicted environmental concentration to the relevant effects endpoint of concern. In this assessment, the resulting toxicity exposure ratios are compared to corresponding levels of concern. A toxicity exposure ratio greater than the level of concern is considered a negligible risk to non-target organisms, whereas a toxicity exposure ratio less than the level of concern indicates some potential risks of concern.

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. As a result of the re-evaluation of fenoxaprop-P-ethyl, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Additional protective equipment to protect mixer/loaders
- A restricted-entry interval to protect workers re-entering treated sites
- A restriction on the amount handled per day
- Application on recreational areas and residential lawns are prohibited
- Application by high pressure handwand is prohibited

Environment

- Additional advisory statements
- Buffer zones for terrestrial habitat

A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. Appendix V lists all proposed label amendments.

What Additional Scientific Information Is Required?

Data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of fenoxaprop-P-ethyl must provide these data or an acceptable scientific rationale to the PMRA within the timeline specified in the decision letter that will be sent to the registrants of the technical active ingredients by the PMRA. Appendix I lists all data requirements.

Next Steps

Before making a final re-evaluation decision on fenoxaprop-P-ethyl, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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

Science Evaluation

1.0 Introduction

Fenoxaprop-P-ethyl is a selective herbicide with contact and systemic action. It is absorbed principally by the leaves, with translocation both acropetally and basipetally to the roots or rhizomes.

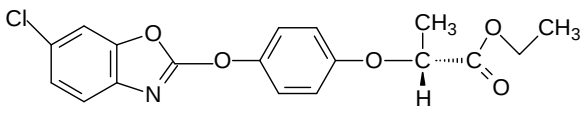
Following the re-evaluation announcement for fenoxaprop-P-ethyl, the registrants of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses included on the labels of commercial end-use products in Canada.

The Pest Management Regulatory Agency (PMRA) conducted a human health risk assessment and used a recent assessment of fenoxaprop-P-ethyl from the European Union (EU) for the environmental risk assessment. The EU document for fenoxaprop-P-ethyl dated November 29, 2007, as well as other information for fenoxaprop-P-ethyl is available at www.efsa.europa.eu.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity

Table 1 Identity of the Technical Grade Active Ingredient

Common name			Fenoxaprop-P-ethyl
Function			Herbicide
Chemical Family			Phenoxy herbicide
Chemical name			
	1	**International Union of Pure and Applied Chemistry (IUPAC)**	ethyl (R)-2-[4-(6-chloro-1,3-benzoxazol-2-yloxy)phenoxy]propionate
	2	**Chemical Abstracts Service (CAS)**	ethyl (R)-2-[4-(6-chlorobenzoxazol-2-yloxy)phenoxy]propionate
CAS Registry Number			71283-80-2
Molecular Formula			$C_{18}H_{16}ClNO_5$
Structural Formula			

Molecular Weight	361.8
Purity of the Technical Grade Active Ingredient	Reg. No. 21903: 95% nominal (limits: 92.2-97.8%) Reg. No. 29250: 96.23% nominal (limits: 95.0-98.5%) Reg. No. 29325: 97.4% nominal (limits: 94-100%) Reg. No. 29380: 97.5% nominal (limits: 95-100%) Reg. No. 29742: 98.0% nominal (limits: 95.06-98.82%)
Registration Number	21903, 29250, 29325, 29380, 29742

Identity of relevant impurities of human health or environmental concern:

There is limited information indicating the presence of dioxins and furans in the technical grade active ingredient (TGAI). Further analysis will be requested from the registrants.

Based on the manufacturing process used, other impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances, are not expected to be present in the product.

2.2 Physical and Chemical Properties

Table 2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 20°C	4×10^{-9} mmHg
UV/Visible spectrum	Not expected to absorb at $\lambda > 300$nm
Solubility in water	0.7 mg/L at pH 5.8
n-Octanol/Water partition coefficient	log $K_{ow} = 4.58$
Dissociation constant	Not applicable

2.3 Use Patterns in Canada and European Union

Canada
Fenoxaprop-P-ethyl is a herbicide registered in Canada to control certain annual and perennial grass weeds in cereals, certain pulse crops, vegetables, certain feed and forage crops, ryegrass grown for seeds, and turfgrass. Currently registered in Canada, there are five technical, two manufacturing concentrate and 16 commercial end-use products containing fenoxaprop-P-ethyl.

They are listed in Appendix II. All current uses are being supported by the registrants and were, therefore, considered in the re-evaluation of fenoxaprop-P-ethyl.
Fenoxaprop-P-ethyl is applied at application rates ranging from 37 to 101 g a.i./ha at one application for field crops and vegetables, at the early growth stage. Applications at the rate of 92 g a.i./ha can be applied up to two times on turfgrass. The end-use products are formulated as an emulsifiable concentrate or a solution and are applied using ground application or aerial (for cereals only) equipment.

European Union
Fenoxaprop-P-ethyl is registered in some EU countries for the control of certain annual and perennial grass weeds in wheat and barley at the application rate of 83 g a.i./ha, via ground application with a maximum of one application per year.

3.0 Impact on Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to fenoxaprop-P-ethyl may occur through consumption of food and water, through residential exposure, while working as a mixer/loader/applicator or by entering treated sites. 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 (for example, children and nursing mothers).

3.1 Toxicological Summary

The PMRA had concluded that technical fenoxaprop-P-ethyl (D isomer) and fenoxaprop-ethyl (D/L racemic mixture) are pharmacokinetically and toxicologically equivalent. Thus, the re-assessment of technical fenoxaprop-P-ethyl has been based on studies conducted with the D isomer, supplemented with additional studies conducted with the D/L racemic mixture where data were lacking (that is, multi-generation reproductive toxicity, and chronic toxicity/carcinogenicity).

Pharmacokinetic studies in rats indicate that orally administered fenoxaprop-P-ethyl is rapidly absorbed from the gastrointestinal tract, widely distributed to tissues and eliminated in the urine and faeces, with females eliminating slightly higher amounts in urine, compared to males; this substance was not detected in expired air. Fenoxaprop-P-ethyl is not bioaccumulative. This substance is rapidly metabolized in both sexes primarily to the free carboxylic acid (eliminated predominantly in faeces) and mercapturic acid (eliminated primarily in urine) of 6-chloro-2,3-dihydro-benzoxazol-2-one.

Fenoxaprop-P-ethyl has low acute toxicity following oral, inhalation, or dermal exposure. Fenoxaprop-P-ethyl induced minimal dermal irritation and mild ocular irritation in rabbits, and was positive for dermal sensitization in guinea-pigs. Acute toxic signs observed following oral and inhalation exposure in rodents included reduced body weight, tremors, disequilibrium, pilo-erection, altered respiration, and coma.

In short-term and long-term toxicity studies in rodents and dogs, treatment-related effects on body weight, lipid metabolism (that is, hypolipidemia characterized by decreased serum cholesterol and serum triglycerides) and effects in the liver and kidney have been consistently observed in all species and by all routes of exposure, though with some species-related variations in sensitivity. Sex-related differences in sensitivity were evident in rats, with males appearing slightly more sensitive to effects in the liver, compared to females. In comparable short-term oral studies, mice appeared to be most sensitive to the toxicological effects of fenoxaprop-P-ethyl, followed by rats and dogs, since degenerative renal and hepatic changes were noted in mice at oral doses which induced less-severe renal and hepatic effects in other species. In longer-term studies, the dog appears to be the most sensitive. The rat was less sensitive to the toxicological effects of fenoxaprop-P-ethyl following dermal and inhalation exposure, compared to oral administration.

With increasing oral dose, fenoxaprop-P-ethyl induces progression of severity of effects in the kidney and liver and reductions in body weight. With increasing duration of exposure to fenoxaprop-P-ethyl, effects have been observed at lower doses in longer-term studies compared to similar effects in studies of shorter duration, suggesting that toxicity increases with increased duration.

In one oral cancer bioassay conducted in mice, there was a statistically significant increase in the incidence of combined adenomas and carcinomas in the liver, and subcapsular B-cell adenomas of the adrenals in males at the highest dose which also induced marked hepatic peroxisomal proliferation, and non-neoplastic changes in the liver (increased organ weight, gross and microscopic lesions) and adrenals (increased organ weight). There is consensus, however, that liver tumours in rodents caused by the demonstrated receptor-based mechanism of action of peroxisome proliferators are of minimal relevance to humans, based on data demonstrating that known rodent peroxisome proliferators do not cause a similar response in the livers of non-human primates or humans. Therefore, based on the weight of evidence, the D/L racemic mixture induces mouse liver tumours by a non-genotoxic mechanism which is not relevant to humans or, at least, for which humans are likely to be much less sensitive.

In a dietary chronic toxicity/carcinogenicity bioassay, there was no increase in peroxisomal proliferation or tumours in Wistar rats exposed to fenoxaprop-ethyl (D/L racemic mixture). Although a higher dose could have been utilized in the long-term rat study, dose-selection was considered adequate based on some evidence of adverse effects in target organs at the highest dose tested, and effect levels in short-term dietary studies conducted in the same strain.

Therefore, it is concluded that there is only limited evidence of carcinogenicity of fenoxaprop-P-ethyl, based on a statistically significant increase in the incidence of adrenal tumours in male (but not female) mice exposed in the diet to high doses of D/L racemic mixture in a single cancer bioassay.

Fenoxaprop-P-ethyl was not genotoxic in core genotoxicity assays including *in-vitro* Ames tests, an *in-vitro* chromosomal aberration assay in human lymphocytes, an *in-vitro* gene mutation assay in hamster cells, and an *in-vivo* bone marrow micronucleus assay in mice. Results were also negative in secondary genotoxicity studies including *in-vitro* assays of unscheduled DNA synthesis in rat hepatocytes, and mutation or mitotic gene conversion in yeast.

Oral developmental toxicity studies in rats and rabbits suggest that there is sensitivity of the young to fenoxaprop-P-ethyl. Skeletal variations in rats (delayed ossification of cranial bones) were observed in the absence of maternal toxicity. Resorptions and severe visceral and skeletal effects in rabbits (kidney displacement, fused and dysplastic sternebrae) were observed in the presence of only slight maternal toxicity. At doses of fenoxaprop-P-ethyl (or D/L racemic mixture) which induce maternal toxicity, increased fetal resorptions, severe visceral malformations (diaphragmatic hernias, abdominal fissures/clefts, protrusion of intestines, kidney displacement, lung lobe fusion, and heart defects) and severe vertebral and sternebrae effects (fragmentations, dislocations, displacements, fusions) were observed in rats and rabbits. These effects are consistent with the known profile for congenital diaphragmatic hernia. Congenital diaphragmatic hernia is a large defect in the posterior or posterolateral region of the diaphragm, near the kidney. Failure in the fusion of the pleuroperitoneal membranes with the other components of the diaphragm results in migration of the intestines, stomach, liver and kidney into the thoracic cavity and displacement of the heart and lungs. Additional malformations were noted at maternally toxic levels in rats, including umbilical hernia, eye defects and unspecified malformations of the head.

There was no clear evidence of reproductive effects or sensitivity of the young in a dietary two-generation reproductive toxicity study in rats conducted with the D/L racemic mixture. Systemic effects at the lowest observed adverse effect level (LOAEL) were similar in pups and parents (including organ weight changes in liver and kidney; nephrocalcinosis, renal pelvic dilation, decreased serum lipids) and were generally consistent with those observed in other oral repeated-dose toxicity studies.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). The calculated MOE is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Where evidence of carcinogenicity is identified for the active ingredient, a cancer potency factor (Q_1*) is generated and used to estimate cancer risk. The product of the expected exposure and the cancer potency factor (Q_1*) estimates the lifetime cancer risk as a probability. A lifetime cancer risk in the range of 1 in 10^{-5} to 1 in 10^{-6} in worker populations is generally considered acceptable.

3.2.1 Toxicology Endpoint Selection for Occupational and Bystander Risk Assessment

3.2.1.1 Dermal Exposure

For assessment of short-term dermal risk for children, an oral two-generation reproductive toxicity study in rats conducted with the D/L racemic mixture was selected. The no observed adverse effect levels (NOAELs) of both parental and offspring were 1.5 mg/kg bw/day. Since young animals in this study were directly exposed for a relatively short period (that is, during lactation and weaning), this investigation is considered most relevant to assessment of short-term risk for children. Though a short-term dermal study in rats is available (NOAEL= 20 mg/kg bw/day), it's use in risk assessment would not be as protective to children, based on an upper-bounding estimate for dermal absorption of 40%. Consistent with effects in the short-term dermal study, effects in the kidney and liver were observed at the LOAEL in parents and offspring (9 mg/kg bw/day) receiving the D/L mixture in the reproductive toxicity study. The target MOE is 100, accounting for standard uncertainty factors of 10x for both interspecies extrapolation and intraspecies variability. No additional PCPA factor has been applied for potential sensitivity of the young since sensitivity appeared to be associated with *in-utero* exposure only.

For assessment of short-and intermediate-term dermal risk for adults, the oral developmental toxicity study in rats with fenoxaprop-P-ethyl was selected, in which a NOAEL of 10 mg/kg bw/day was derived based on skeletal effects (delayed ossification of cranial bones) in offspring at 32 mg/kg bw/day, in the absence of maternal toxicity. Although only one site was developmentally delayed, the importance of the site (cranium) along with the prominance of developmental toxicity throughout the database for the D isomer and D/L mixture contributed to the weight of evidence in using this endpoint for risk assessment. The target MOE is 300, accounting for standard uncertainty factors of 10x for both interspecies extrapolation and intraspecies variability and an additional PCPA factor of 3x for significant effects in the young in the absence of maternal toxicity.

Since the oral toxicity of fenoxaprop-P-ethyl increases with increasing duration of exposure and long-term dermal studies have not been identified, the long-term dermal risk assessment has been conducted based on the chronic dietary assay in dogs. In this study, reduced body weight gain, haematological changes and increased relative kidney and liver weights were observed at the LOAEL of 1.9 mg/kg bw/day; the NOAEL in this study was 0.4 mg/kg bw/day. The target MOE is 100, accounting for standard uncertainty factors of 10x for interspecies extrapolation and 10x for intraspecies variability. This NOAEL and MOE are considered inherently protective of potential developmental effects.

3.2.1.2 Inhalation Exposure

Although a short-term inhalation study was available, it's use in risk assessment would not be protective to children or for females 13+, hence the risk assessment has defaulted to the use of oral studies. For assessment of short-term inhalation risk for children, the oral two-generation reproductive toxicity study in rats conducted with the D/L racemic mixture has been selected. Since young animals in this study were directly exposed (during lactation and weaning) for a relevant duration, this investigation is considered most appropriate for assessment of short-term risk for children. Consistent with effects in repeated-dose inhalation studies conducted with the D+ isomer (NOAEL= 19 mg/kg bw/day), effects in the kidney and liver were observed at the LOAEL in parents and offspring (9 mg/kg bw/day) receiving the D/L mixture. The parental and offspring NOAEL in the reproductive toxicity study was 1.5 mg/kg bw/day. The target MOE is 100, accounting for standard uncertainty factors of 10x for both interspecies extrapolation and intraspecies variability. No additional factor has been applied for potential sensitivity of the young since sensitivity appears to be associated with *in-utero* exposure only.

For assessment of short- or intermediate-term inhalation risk for adults, the oral developmental toxicity study in rats with fenoxaprop-P-ethyl was selected, in which a NOAEL of 10 mg/kg bw/day was derived based on skeletal effects (delayed ossification of cranial bones) in offspring at 32 mg/kg bw/day, in the absence of maternal toxicity. The target MOE is 300, accounting for standard uncertainty factors of 10x for both interspecies extrapolation and intraspecies variability, with an additional factor of 3x applied for significant toxicity in the young in the absence of maternal toxicity.

Since the oral toxicity of fenoxaprop-P-ethyl increases with increasing duration of exposure and long-term inhalation studies were not identified, the long-term inhalation risk assessment was based on the NOAEL of 0.4 mg/kg bw/day for fenoxaprop-ethyl (D/L racemic mixture) which was derived in an adequate 2-year oral toxicity study in dogs. Reduced body weight gain, haematological changes and increased relative kidney and liver weights were noted at the LOAEL of 1.9 mg/kg bw/day. The target MOE is 100, accounting for standard uncertainty factors of 10x for both interspecies extrapolation and intraspecies variability. This NOAEL and MOE are considered inherently protective of potential developmental effects.

3.2.1.3 Non-Dietary Oral Ingestion

Acute oral reference doses (1-day) were not required due to the low acute toxicity of fenoxaprop-P-ethyl. For short-term exposure (1-30 days), the oral two-generation reproductive toxicity study in rats receiving the D/L racemic mixture was selected, in which parental and offspring NOAEL's of 1.5 mg/kg bw/day were derived. Since young animals in this study were directly exposed during lactation and weaning for a relevant duration, this investigation is considered most relevant to assessment of short-term risk for children. The target MOE is 100, accounting for standard uncertainty factors of 10x for both interspecies extrapolation and intraspecies variability. No additional PCPA factor has been applied for potential sensitivity of the young since sensitivity appeared to be associated with *in-utero* exposure only.

3.2.1.4 Cancer Risk Assessment

The results considered most pertinent to the re-evaluation of the carcinogenicity of fenoxaprop-P-ethyl are the increased incidences of adrenal subcapsular B-cell adenomas in male mice exposed in the diet to fenoxaprop-ethyl (D/L racemic mixture). An adjusted Q* value of 8.7 $x10^{-2}$ $(mg/kg\ bw/day)^{-1}$ has been derived by PMRA for adrenal tumours in male mice.

3.2.1.5 Dermal Absorption

A dermal absorption value of 40% was used in route-to-route extrapolation for the re-evaluation of fenoxaprop-P-ethyl.

The toxicology endpoints used in the risk assessment for fenoxaprop-P-ethyl are summarized in Appendix III.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to fenoxaprop-P-ethyl through mixing, loading or applying the pesticide, and when entering a treated site to conduct activities such as scouting and/or irrigating treated crops.

Mixer/Loader/Applicator
There are potential exposures to mixers, loaders, and applicators. Estimates of mixer/loader/applicator (M/L/A) exposure were based on the best available data at this time. Handler exposure analyses were performed using the Pesticide Handlers Exposure Database (PHED), Outdoor Residential Exposure Task Force (ORETF) data was used for low pressure turf gun, assuming the label recommended personal protective equipment (PPE). Maximum application rates were used in the assessment. The NOAEL value of 10 mg/kg bw/day from a rat oral developmental toxicity study was selected as the short-term endpoint for both occupational dermal and inhalation exposure. A default body weight of 70 kg, a dermal absorption value of 40% and PMRA default values for area treated per day were used in the assessment.

The exposure estimates (ranging 799 to 30420) for mixer/loader exceed the target MOE of 300 (Appendix IV, Table 1).

Occupational cancer risk was calculated assuming 40 years of exposure over a 75 year lifetime.

Results of the fenoxaprop-P-ethyl M/L/A exposure cancer risk assessment are summarized in Appendix IV, Table 2.

Postapplication Exposure and Risk
The postapplication occupational risk assessment considers exposures to workers entering treated sites. Based on fenoxaprop-P-ethyl use pattern, there is potential for short-term (< 30 days) postapplication exposure to fenoxaprop-P-ethyl residues for workers.

Inhalation exposure was considered negligible because fenoxaprop-P-ethyl is non-volatile, hence this route of exposure was not considered.

Default dislodgeable foliar residue (DFR) values and activity specific transfer coefficients (TC) were used to estimate postapplication exposure resulting from contact with treated foliage at various times after application. DFR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. A TC is a factor that relates worker exposure to transferrable residues. TCs are specific to a given crop and activity combination (for example, hand harvesting apples, scouting late season corn) and reflect standard agricultural work clothing worn by adult workers. Postapplication exposure activities include harvesting, thinning, pruning, scouting and irrigating crops.

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE (> 300 for short-term dermal exposure scenarios for fenoxaprop-P-ethyl).

For dermal exposure, since no appropriate chemical-specific DFR studies are currently available, the default value of 20% of the application rate for agricultural crops and 5% of the application rate for turfgrass were used in the assessment. A daily default dissipation rate of 10% was used for all crops.

All calculated occupational postapplication non-cancer MOEs at Day 0 were greater than the target MOE of 300 (Appendix IV, Table 3).

A cancer risk assessment was conducted for re-entry work in crops recently treated with fenoxaprop-P-ethyl using a linear-low-dose extrapolation approach. A time-weighted average (TWA) dislogeable foliar residue (DFR) values were calculated by averaging DFR values for a 30-day period starting at Day 0. Results of the fenoxaprop-P-ethyl postapplication exposure cancer risk assessment were summarized in Appendix IV, Table 4. The cancer risk at Day 0 for most of the scenarios was below the threshold of 1×10^{-5}. REIs that result in a cancer risk of less than 1×10^{-5} ranged from 2 to 4 days for the remaining scenarios.

3.2.3 Non-Occupational Exposure and Risk Assessment

Non-occupational exposure to fenoxaprop-P-ethyl was conducted for turf scenario only since the remaining uses are on agricultural crops.

An assessment of non-occupational (residential) handler exposure was not conducted because no domestic products are registered in Canada.

Non-Occupational Postapplication Exposure
Exposure and risk estimates for postapplication activities on turf treated in recreational areas (for example, public areas, school yards, parks) and golf courses were conducted. Inhalation exposure was considered negligible because fenoxaprop-P-ethyl is non-volatile, hence this route of exposure was not considered. For youth and adults, dermal exposure was assessed. For children, hand-to-mouth, object-to-mouth and soil ingestion were also considered.

Since no appropriate chemical-specific DFR studies are currently available, the default value of 20% for object-to-mouth scenario, an application rate of 5% for the remaining scenarios, and a daily default dissipation rate of 10% were used in the assessment. Exposure times were two hours for recreation, and four hours for playing golf. For adults, a NOAEL value of 10 mg/kg bw/day, with a target MOE of 300 were selected, and for children, an NOAEL value of 1.5 mg/kg bw/day, with a target MOE of 100 were selected (Appendix III, Toxicology Endpoints for Health Risk Assessment of Fenoxaprop-P-ethyl).

The results of the fenoxaprop-P-ethyl residential postapplication non-cancer risk assessment are summarized in Appendix IV, Table 5. The calculated risks for youth and adults from postapplication exposure were greater that the target MOEs of 100 and 300, respectively, and therefore were not of concern. However, the calculated postapplication risk for children was below the target MOE of 100 and therefore was of concern.

As per Section 3.2.1, cancer risks were calculated using a linear low-dose extrapolation approach. Results of the fenoxaprop-P-ethyl postapplication exposure cancer risk assessment are summarized in Appendix IV, Table 6. Cancer risk from postapplication exposure was below the threshold of 1×10^{-6} for the golfing scenario and therefore was not of concern. However, cancer risk was above the threshold of 1×10^{-6} for the recreational scenario and therefore was of concern.

3.3 Exposure From Food and Drinking Water

3.3.1 Determination of Acute Reference Dose

The assessment has been based on teratogenic effects in developmental toxicity studies conducted with fenoxaprop-P-ethyl, assuming these effects may arise from a single exposure. The acute reference dose (ARD) is relevant to women of child-bearing age; no ARD has been established for other populations due to the low acute toxicity of fenoxaprop-P-ethyl.

The NOAEL (32 mg/kg bw/day) for teratogenic effects of fenoxaprop-P-ethyl in the oral developmental study in rabbits was selected. This NOAEL was based on visceral anomalies and severe skeletal effects in offspring at 100 mg/kg bw/day, in the presence of slight maternal toxicity. Consistent evidence of teratogenicity has been presented in developmental toxicity studies conducted with either fenoxaprop-P-ethyl or the D/L mixture. An uncertainty factor of

300 has been applied to the NOAEL to account for inter-species extrapolation (10x), inter-species variability (10x), with an additional PCPA factor of 3x for severity of effects in offspring at levels causing only slight maternal toxicity. The ARD was calculated to be 0.1 mg/kg bw.

3.3.2 Determination of Acceptable Daily Intake

An ADI has been derived based on the NOAEL of 0.4 mg/kg bw/day for fenoxaprop-ethyl (D/L racemic mixture) in a 2-year oral toxicity study in dogs, in which reduced body weight gain, haematological changes and increased relative kidney and liver weights were observed in both sexes at the LOAEL of 1.9 mg/kg bw/day. Application of a total uncertainty factor of 100 (10x for interspecies extrapolation and 10x for intraspecies variability) to the NOAEL results in an ADI of 0.004 mg/kg bw/day. This value is inherently protective of potential developmental effects as it provides a margin of safety of >2000 to developmental NOAEL's.

3.3.3 Dietary Exposure and Risk Assessment

Chronic and acute dietary risk assessments for fenoxaprop-P-ethyl were conducted using endpoints outlined in Appendix III (ADI = 0.004 mg/kg bw/day, ARD = 0.1 mg/kg bw, $Q_1^* = 8.7 \times 10^{-2}$ (mg/kg bw/day)$^{-1}$). The following outlines the dietary risk assessment conclusions:

The refined assessment found that chronic exposure to fenoxaprop-P-ethyl from food and water was below the level of concern and considered acceptable; 0.1% to 0.3% of the ADI for all population subgroups. Acute exposure to fenoxaprop-P-ethyl from food and water was below the level of concern and considered as acceptable; 0.02% of the ARD for the most sensitive subgroup, females 13-49 years old. The lifetime cancer risk estimate for general population from exposure to fenoxaprop-P-ethyl in food and water was below the threshold of 1 x 10^{-6}.

Maximum Residue Limits
No Maximum Residue Limits (MRLs) have been established in Canada. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL will be implemented in the future, as indicated in the December 2009 Information Note, *Progress on Minimizing Reliance on the 0.1 Parts per Million as a General Maximum Residue Limit for Food Pesticide Residue*.

3.4 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to fenoxaprop-P-ethyl. Acute and chronic aggregate risk assessments are comprised of contributions from food and drinking water exposures. Short-term and intermediate aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal, inhalation).

Aggregate risk assessments were only conducted for golfers. Aggregate non-cancer MOEs were significantly greater than the target MOEs (Appendix IV, Table 7), and aggregate cancer risks were below the threshold of 1 x 10^{-6} (Appendix IV, Table 8), and therefore, it is not of concern.

3.5 Health Risk Mitigation

Based on the exposure assessments described in Table 1, 2, 3, 4, 5, and 6 of Appendix IV, recommendations to mitigate exposure includes the following:

- Gloves must be worn during mixing and loading for all uses;
- Restrictions on the amount of fenoxaprop-P-ethyl handled per day for uses on potatoes, lentils, flax, sunflower, feed and forage crops (that is, custom M/L/A: approx. 22 kg a.i./day or 220 ha at the rate of 101 g a.i./ha);
- The following REIs are required:

Crop	Activity	REI (days)
Flax	Scouting	2
Broccoli, cabbage, cauliflower	Thinning, scouting, irrigation	4
Turfgrass, sod farms and golf courses	Harvesting, mowing, transplanting	3

For turf uses, the following are not supported:

- Application by high pressure handwand
- Use in recreational and residential areas

4.0 Impact on the Environment

4.1 Environmental Fate

The European Food Safety Authority (EFSA) of the EU published a risk assessment of fenoxaprop-P in 2007. The environmental risk assessment conclusions are outlined below.

Fenoxaprop-P-ethyl was not found to be persistent in soil under aerobic conditions and was rapidly converted to fenoxaprop-P, which has low to moderate persistence. The major transformation product of fenoxaprop-P is chlorobenzoxazolonze, which is also found to have low to moderate persistence. Fenoxaprop-P-ethyl was immobile in soil, while fenoxaprop-P and chlorobenzoxazolonze has medium to low mobility. Hydrolysis of fenoxaprop-P-ethyl and fenoxaprop-P is pH dependent, while chlorobenzoxazolonze is hydrolytically stable. Fenoxaprop-P-ethyl was found to be photo-transformed in water. Long term transport of fenoxaprop-P-ethyl and fenoxaprop-P through the atmosphere is not expected based on their low vapour pressures.

4.2 Environmental Risk Assessment

To assess the ecological risk of fenoxaprop-P-ethyl to both aquatic and terrestrial non-target plants and animals, the EFSA calculated toxicity exposure ratios (TER) based on appropriate toxicity endpoints and predicted environmental concentration (PEC) and compared the resulting TERs to corresponding trigger values. The risk is considered negligible to non-target organisms if the calculated TER is greater than the trigger value.

In the EFSA's assessment, the calculation of predicted environmental concentration was based on one ground application at a rate of 83 g a.i./ha. The EFSA determined the following:

- Chronic TERs exceeded the trigger values for birds, mammals, aquatic organisms, insects, other non-target arthropods, and soil non-target micro-organisms, indicating that risks of concern were expected to be low.

- The chronic TER was below the trigger value for terrestrial non-target plants, indicating a risk of concern. The EFSA required mitigation measures to protect terrestrial non-target plants, consisting of a 5-metre buffer zone, or the use of drift reducing nozzles (reducing the drift by ≥ 50%) and a buffer zone of one metre.

There are some use differences between Canada and the EU:

- The maximum application rate in Canada is 101 g a.i./ha on vegetables, which is approximately 22% higher than the rate assessed by the EFSA (83 g a.i./ha on cereals);
- Fenoxaprop-P-ethyl can be applied up to two times per year on turf grass in Canada;
- Fenoxaprop-P-ethyl can be applied aerially on cereals in Canada.

It is noted that the risk estimates generated by the EFSA were significantly above the trigger values indicating no risk concerns with mitigation measures. In addition, aerial application on cereals and turf use were included in the PMRA's buffer zone calculations in this re-evaluation. Therefore, the differences in use pattern between Canada and the EU should not result in significantly higher risk in Canada. On this basis, the EFSA's conclusions are considered relevant to the Canadian situation.

For end use products registered for uses on barley and wheat, the following buffer zones are required.

Method of application	Buffer zone (metres) required	
	Aquatic Habitat	Terrestrial Habitat
Field Spray	0	1
Aerial	0	20

Based on PMRA general practices, the following label statement are required on all end-use products:

- Advisory statements, and statements regarding runoff and contamination of groundwater

The proposed label amendments are listed in Appendix V.

4.3 Pest Control Product Policy Considerations

4.3.1 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, namely, CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative).

During the re-evaluation process, fenoxaprop-P-ethyl was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy,* and evaluated against the Track 1 criteria for persistence and bioaccumulation. In order for fenoxaprop-P-ethyl or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met.

Fenoxaprop-P-ethyl does not meet the Track 1 criterion for persistence, as its DT_{50} values in air (13.4 hours), water (0.6 – 23.3 days), and soil (0.02 – 0.8 days), are below the cut-off value of 180 days. Fenoxaprop-P-ethyl does not meet the Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (Log K_{ow} = 4.58) and BCF (338 in whole fish) are below the Track 1 criteria. On this basis, it is concluded that the use of fenoxaprop-P-ethyl is not expected to result in the entry of Track 1 substances in the environment.

4.3.2 Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of fenoxaprop-P-ethyl contaminants in the technical are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03; and DIR2006-02, 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 conclusion:

There is limited information indicating the presence of dioxins and furans in the technical grade active ingredient. Analysis for dioxins and furans will be requested from the registrants.

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

5.0 Incident reports

Starting April 26, 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame.

Available information from the PMRA database indicates that one incident report was submitted. The report was listed as "human minor" and occurred in Canada. Eye irritation was reported, however, protective eye equipment, as required on the label, was not worn.

6.0 Proposed Re-evaluation Decision

The PMRA has determined that fenoxaprop-P-ethyl is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use product must be amended to include the label statements listed in Appendix V. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. The registrant of the technical grade active ingredient is required to submit data as a condition of continued registration under Section 12 of the *Pest Control Products Act*. Appendix I lists data requirements.

7.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, *Pest Management Regulatory Agency Re-evaluation Program,* and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at www.healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The EFSA of EU document for fenoxaprop-P-ethyl is available at www.efsa.europa.eu.

List of Abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
ARI	aggregate risk index
bw	body weight
CAS	Chemical Abstracts Service
DACO	data code
DT_{50}	dissipation time to 50%
EFSA	European Food Safety Authority
EU	European Union
g	gram(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LOAEL	lowest observed adverse effect level
mg	milligram(s)
mm	millimetre(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
NOAEL	no observed adverse effect level
PCPA	*Pest Control Products Act*
PEC	Predicted environmental concentration
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PHI	preharvest interval
p*K*a	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
PRVD	Proposed Re-evaluation Decision
Q_1*	cancer potency factor
REI	restricted-entry interval
RfD	reference dose
RVD	Re-evaluation Decision
TC	transfer coefficient
TER	Toxicity exposure ratio
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
UV	ultraviolet

Appendix I Additional Data Requirements

The following data are required as a condition of continued registration under Section 12 of the *Pest Control Products Act*. The registrants of technical products are required to provide these data within the timeline specified in the decision letter that will be sent to registrants by the PMRA.

DACO 2.13.4 Impurities of human health or environmental concern

The registrants of products Reg. No. 21903, Reg. No. 29250, Reg. No. 29325 and Reg. No. 29742 must submit recent analytical data from at least five batches of TGAI for all identifiable dioxins and furans, from a GLP-compliant or government-accredited laboratory. The report should include data for the 17 substances listed in Table 4 of the Priority Substances List 1 document "Polychlorinated dibenzodioxins and polychlorinated dibenzofurans", found at: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl1-lsp1/dioxins_furans_dioxines_furannes/index-eng.php. The analytical method(s) used must utilize the lowest practical limits of quantitation and be fully specified, either by reference to a standard method or by inclusion of a detailed description together with validation data.

Appendix II Registered Products Containing Fenoxaprop-P-ethyl as of October 14, 2010

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
21903	Technical	Bayer CropScience Inc.	Fenoxaprop-P-ethyl Technical Herbicide	Solid	95%
29250	Technical	Makhteshim-Agan of North America Inc.	MANA Fenoxaprop-p ethyl Technical Herbicide	Solid	97.46%
29325	Technical	Cheminova Canada Inc.	Cheminova Fenoxaprop-P-ethyl Technical	Solid	97.4%
29380	Technical	Nufarm Limited	A H Marks Fenoxaprop-P-ethyl Technical Ester	Solid	97.5%
29742	Technical	NewAgco Inc.	NewAgco Fenoxaprop-P-ethyl Herbicide Technical	Solid	98.0%
24297	Manufacturing concentrate	Bayer CropScience Inc.	Fenoxaprop-P-ethyl EW Manufacturing Concentrate	Suspension	67 g/L
24775	Manufacturing concentrate	Bayer CropScience Inc.	Fenoxaprop-P-ethyl EC Manufacturing Concentrate	Emulsifiable concentrate	80.5 g/L
21914	Commercial	Bayer CropScience Inc.	Excel Super Post-emergent Herbicide	Emulsifiable concentrate	80.5 g/L
21925	Commercial	Bayer CropScience Inc.	Acclaim Super EW Herbicide	solution	67 g/L
22205	Commercial	Bayer CropScience Inc.	Excel Super Herbicide	Emulsifiable concentrate	80.5 g/L
22845	Commercial	Bayer CropScience Inc.	Component #1 Post-Emergent Herbicide (Fusion Tank Mix)	Emulsifiable concentrate	80.5 g/L
22886	Commercial	Bayer CropScience Inc.	Acclaim Super EC Herbicide	Emulsifiable concentrate	80.5 g/L
25511	Commercial	Bayer CropScience Inc.	Puma Super Emulsifiable Concentrate Post-Emergent Herbicide	Emulsifiable concentrate	92 g/L
25864	Commercial	Bayer CropScience Inc.	Puma 120 Super Emulsifiable Concentrate Post-Emergent Herbicide	Emulsifiable concentrate	120 g/L
29151	Commercial	Bayer CropScience Inc.	Wildcat Herbicide	Emulsifiable concentrate	120 g/L
29152	Commercial	Bayer CropScience Inc.	Panther Herbicide	Emulsifiable concentrate	120 g/L
29153	Commercial	Bayer CropScience Inc.	Pumax Herbicide	Emulsifiable concentrate	120 g/L
29268	Commercial	Makhteshim-Agan of North America Inc.	Bengal 120 EC	Emulsifiable concentrate	120 g/L
29367	Commercial	Bayer CropScience Inc.	Tundra Herbicide	Emulsifiable concentrate	46 g/L
29273	Commercial	Interprovincial Cooperative Limited	IPCO Fenoxaprop-P-ethyl 120 EC	Emulsifiable concentrate	120 g/L
29494	Commercial	Nufarm Limited	Cordon	Emulsifiable concentrate	120 g/L

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
29488	Commercial	Bayer CropScience Inc.	Puma Advance EC Herbicide	Emulsifiable concentrate	90 g/L
29615	Commercial	Bayer CropScience Inc.	Puma Advance Herbicide	Emulsifiable concentrate	90 g/L

Appendix III Toxicology Endpoints for Health Risk Assessment of Fenoxaprop-P-ethyl

EXPOSURE SCENARIO	ENDPOINT	STUDY	DOSE (mg/kg bw/day)	UF or MOE[a]
Acute Dietary	teratogenicity (visceral and skeletal effects) with only slight maternal toxicity	oral developmental toxicity - rabbits	32 mg/kg bw/day fenoxaprop-P-ethyl	300
	ARD = 0.1 mg/kg bw			
Chronic Dietary	haematological and body weight changes, kidney and liver effects	chronic dietary - dogs	0.4 mg/kg bw/day fenoxaprop-ethyl (D/L racemic mixture)	100
	ADI = 0.004 mg/kg bw/day			
Short-Term[b] and Intermediate-Term[c] Dermal[e] and Inhalation[f] (Adults)	skeletal variations without maternal toxicity	oral developmental toxicity - rats	10 mg/kg bw/day fenoxaprop-P-ethyl	300
Short-Term[b] Dermal[e] and Inhalation[f] (Children)	liver and kidney changes	dietary 2-generation reproductive toxicity study - rats	1.5 mg/kg bw/day fenoxaprop-ethyl (D/L racemic mixture)	100
Long-Term[d] Dermal[e] and Inhalation[f]	haematological and body weight changes, kidney and liver effects	chronic dietary - dogs	0.4 mg/kg bw/day fenoxaprop-ethyl (D/L racemic mixture)	100
Short-Term[b] Non-Dietary Oral Ingestion	liver and kidney changes	dietary 2-generation reproductive toxicity study - rats	1.5 mg/kg bw/day fenoxaprop-ethyl (D/L racemic mixture)	100
Cancer[g]			$Q_1^* = 8.7 \times 10^{-2}$ (mg/kg bw/day)$^{-1}$	

[a] UF refers to total of uncertainty factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments
[b] Duration of exposure is 1 to 30 days
[c] Duration of exposure is 1 to several months
[d] Duration of exposure is several months to lifetime
[e] Since an oral NOAEL was selected, a dermal absorption factor of 40% was used in route-to-route extrapolation
[f] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) was used in route-to-route extrapolation
[g] The cancer risk estimate is adjusted for body weight

Appendix IV Agricultural Mixer/Loader/Applicator Risk Assessment

Table 1 Occupational (mixer/loader/applicator) Non-Cancer Exposure and Risk Assessment

Crop	Application Equipment	Application Rate (g a.i./ha)	Area Treated/day[a] (ha)	M/L/A Unit exposure[b] (µg/kg a.i.)		Daily Exposure[c] (µg/kg bw/day)	MOE[d] (target = 300)
				Dermal	Inhalation		
Personal Protective Equipment: M/L: coveralls over long sleeved shirt, long pants, gloves; A: coveralls over single layer cloth							
Spring and durum wheat, spring barley	M/L (liquid, open).	92	400	32.77	1.6	7.73	1293
	Aerial, liquid application			9.66	0.07	2.07	4831
Rapeseed, peas, tame buckwheat and tame mustard	Custom applicator M/L (liquid, open). Groundboom, open cab	89	360	53.81	2.56	11.02	907
				53.81	1.12 (with respirator[e])	10.33	968
	Farmer applicator M/L (liquid, open). Groundboom, open cab		107	53.81	2.56	3.08	3247
				53.81	1.12 (with respirator[e])	2.87	3484
Canola, flax, field peas, lentils, mustard	Custom applicator M/L (liquid, open). Groundboom, open cab	37	360	53.81	2.56	4.41	2268
				53.81	1.12 (with respirator[e])	2.94	3401
	Farmer applicator M/L (liquid, open). Groundboom, open cab		107	53.81	2.56	1.31	7634
				21.04	0.96 (with respirator[e])	0.41	6173
Potatoes, lentils, flaxes, sunflower, (seedling alfalfa, red clover, alsike clover, white clover, sweet clover, sainfoin, bird's foot trefoil, cicer milkvetch for seed and forage)	Custom applicator M/L (liquid, open). Groundboom, open cab	101	360	53.81	2.56	12.51	799
	Farmer applicator M/L (liquid, open). Groundboom, open cab		107	53.81	2.56	3.28	2717

Table 1 Occupational (mixer/loader/applicator) Non-Cancer Exposure and Risk Assessment (cont'd)

Crop	Application Equipment	Application Rate (g a.i./ha)	Area Treated/day[a] (ha)	M/L/A Unit exposure[b] (µg/kg a.i.)		Daily Exposure[c] (µg/kg bw/day)	MOE[d] (target = 300)
				Dermal	Inhalation		
Broccoli, cabbage, cauliflower, onions	Custom and Farmer applicator M/L (liquid, open). Groundboom, open cab	101	26	53.81	2.56	0.81	10989
Dry common beans, soybeans	Custom applicator M/L (liquid, open). Groundboom, open cab	54	360	53.81	2.56	6.69	1495
	Farmer applicator M/L (liquid, open). Groundboom, open cab		107	53.81	2.56	1.99	5025
Tomatoes, asparagus, carrots	Custom and Farmer applicator M/L (liquid, open). Groundboom, open cab		26	53.81	2.56	0.43	20833
Ryegrass growing for seed	Custom applicator M/L (liquid, open). Groundboom, open cab	92	360	6299.66 (without gloves)	2.56	1193.47	8
				53.81	2.56	11.39	878
	Farmer applicator M/L (liquid, open). Groundboom, open cab		107	6299.66 (without gloves)	2.6	354.73	28
				53.81	2.56	3.39	2950

Table 1 Occupational (mixer/loader/applicator) Non-Cancer Exposure and Risk Assessment (cont'd)

Crop	Application Equipment	Application Rate (g a.i./ha)	Area Treated/day[a] (ha)	M/L/A Unit exposure[b] (µg/kg a.i.)		Daily Exposure[c] (µg/kg bw/day)	MOE[d] (target = 300)
				Dermal	Inhalation		
Turfgrasses	Sod farms, M/L (liquid, open). Groundboom, open cab	92	30	53.81	2.56	0.96	10526
	Golf courses, M/L (liquid, open). Groundboom, open cab		16	53.81	2.56	0.51	19736
	Sod farms, golf courses and recreational and residential lawns, M/L (liquid, open). Low pressure turf gun		2	301[f]	4[f]	0.29	30420
	Golf courses and recreational and residential lawns, High-pressure handwand (Applicator) (light inhalation)	0.11 g a.i./L (max. of 1.14 L/ha of product @ 800 L water/ha)	3750 L/day	2453.52	151.00	6.96	1437
	Golf courses, recreational and residential lawns, backpack sprayer (Applicator) (moderate inhalation)	0.23 g a.i./L (max. of 1.14 L/ha of product @ min. 400 L water/ha)	150 L/day	2629.77	64.60	0.58	17241

[a] Area treated per day are based on the PMRA's in-house Exposure Re-evaluation Section default values.
[b] Canadian PHED version 1.1, February 2002.
[c] Dermal exposure was calculated as: unit exposure x dermal absorption value x application rate x daily area treated / body weight (70 kg)
Inhalation exposure was calculated as: unit exposure x application rate x daily area treated / body weight (70 kg)
Dermal absorption value: 40%
[d] MOE was calculated as: NOAEL / daily dose
[e] a protection factor of 90% is assumed if respirator was used
[f] ORETF data

Table 2 Occupational (mixer/loader/applicator) Cancer Risk Estimates

Crop	Application Method	Application Rate (g a.i./ha)	Area Treated Per Day [a] (ha)	Absorbed Daily Dose[b] (µg/kg bw/day)	Lifetime Average Daily Dose[c] (mg/kg bw/day)	Risk[d]
Spring and durum wheat, spring barley	Aerial, (M/L)	92	318	6.15	1.35E-04	1E-05
	Aerial (A)			1.65	3.61E-05	3E-06
Rapeseed, peas, tame buckwheat and tame mustard	Groundboom (custom)	89	240	7.35	1.61E-04	1E-05
				6.89 (with respirator)	1.51E-04	1E-05
	Groundboom (farmer)		60	1.73	2.52E-06	2E-07
				1.61 (with respirator)	2.35E-06	2E-07
Canola, flax, field peas, lentils, mustard	Groundboom (custom)	37	240	2.94	6.45E-05	6E-06
				1.96 (with respirator)	4.29E-05	4E-06
	Groundboom (farmer)		60	8.73	1.21E-07	1E-08
				0.27 (with respirator)	3.99E-07	3E-08
Potatoes, lentils, flaxes, sunflower, Seedling alfalfa, red clover, alsike clover, white clover, sweet clover, sainfoin, bird's foot trefoil, cicer milkvetch for seed and forage	Groundboom (custom)	101	240	8.34	1.83E-04	2E-05
			220	7.65	1.68E-04	1E-05
	Groundboom (farmer)		60	2.19	3.19E-06	3E-07
Broccoli, cabbage, cauliflower, onions (dry bulb)	Groundboom (custom)	101	12	0.37	8.21E-06	7E-07
	Groundboom (farmer)			0.37	5.45E-07	5E-08
Dry common beans, soybeans	Groundboom (custom)	54	240	4.46	9.80E-05	9E-06
	Groundboom (farmer)		60	1.12	1.94E-06	1E-07
Tomatoes, asparagus, carrots	Groundboom (custom)	54	12	0.20	4.35E-06	4E-07
	Groundboom (farmer)			0.20	2.90E-07	3E-08
Ryegrass growing for seed	Groundboom (custom)	92	240	795.33 (without gloves)	1.75E-02	2E-03
				7.59	1.67E-04	1E-05
	Groundboom (farmer)		60	200.60 (without gloves)	2.93E-04	3E-05
				1.90	2.78E-06	2E-07

Table 2 Occupational (mixer/loader/applicator) Cancer Risk Estimates (cont'd)

Crop	Application Method	Application Rate (g a.i./ha)	Area Treated Per Day (ha)	Absorbed Daily Dose[a] (µg/kg bw/day)	Lifetime Average Daily Dose[b] (mg/kg bw/day)	Risk[c]
Turfgrass	Sod farms,Groundboom	92	30	0.96	4.21E-05	4E-06
	Golf courses,Groundboom		16	0.51	2.22E-05	2E-06
	Sod farms, golf courses and recreational and residential lawns, Low pressure turf gun		2	0.29	1.27E-05	1E-06
	Golf courses and recreational and residential lawns, High-pressure handwand (Applicator) (light inhalation)	0.11 g a.i./L (max. of 1.14 L/ha of product @ min. 400 L water/ha)	3750 L/day	6.96	3.09E-04	3E-05
	Golf courses and recreational and residential lawns, backpack sprayer (Applicator) (moderate inhalation)	0.23 g a.i./L (max. of 1.14 L/ha of product @ min. 400 L water/ha)	150 L/day	0.58	2.54E-05	2E-06

[a] Based on the 95th percentile of far size from Stats Canada 2006 Census of Agriculture data. Custom applicators were assumed to treat 6 farms per day.

[b] Absorbed Daily Dose = daily dermal dose + daily inhalation dose, as determined by PHED scenarios in Table 2, except for using low pressure turf gun on sod farms, golf courses and lawn, exposure unit value were used ORETF data.

[c] LADD = ADD x treatment frequency x working duration / (365 days/year x life expectancy (75 years)).

Where treatment frequency = 15 days for custom applicators for agricultural uses; 1 day for farmer applicators for agricultural uses; 30 days for applicators to turfgrass.

Working duration = 40 years (NAFTA, 1999).

[d] A Q_1* value of 0.087 (mg/kg/day) was considered appropriate to use in the cancer risk assessment.

Table 3 Occupational Post-Application Non-Cancer Risk Estimates, MOEs (at Day 0)

Crop	Application rate (g a.i./ha)	Re-entry activity	Transfer coefficient[a] (cm^2/hour)	Dislodgeable residue (µg/cm^2)	Dermal Exposure[b] (mg/kg bw/day)	MOE (target=300)
Wheat, barley	92	Irrigation, scouting	1500	0.184	0.0126	793
Rapeseed, canola, tame buckwheat, tame mustard, lentils	89	Irrigation, scouting	1500	0.178	0.0122	820
Peas, beans	89	Irrigation, scouting	1500	0.178	0.01221	820
Flax	101	Scouting	1500	0.202	0.0139	719
Broccoli, cabbage, cauliflower	101	Thinning, scouting, irrigation	2000	0.202	0.0185	540
Onions (dry bulb)	101	Irrigation, scouting, thinning	300	0.202	0.00277	3610
Sunflower	101	Scouting	1000	0.202	0.00923	1083
Asparagus	54	Irrigation, scouting	500	0.108	0.00247	4049
Carrots	54	Irrigation, scouting	300	0.108	0.00148	6757
Soybeans	54	Irrigation, scouting	1500	0.108	0.00741	1350
Tomatoes	54	Staking, thinning, training, tying	1000	0.108	0.00494	2024
		Irrigation, scouting	700		0.00346	2890
Potatoes	101	Irrigation, scouting	1500	0.202	0.00923	1083
Seedling alfalfa, red clover, alsike clover, white clover, sweet clover, sainfoin, bird's foot trefoil, cicer milkvetch for seed and forage	101	Irrigation, scouting	1500	0.202	0.00923	1083
Ryegrass, growing for seed	92	Irrigation, scouting	1500	0.184	0.0126	793
Turfgrass, sod farms, golf courses	92	Harvesting, mowing, transplanting	6800	0.0505	0.01570	637
		Scouting, irrigation, fertilizing, aerating, hand pruning, seeding treated turf	500		0.000114	87719

[a] USEPA Policy # 003.1, Agricultural Transfer Coefficients, revised August 7, 2000.

[b] Dermal exposure was calculated as: DFR x application rate x dermal absorption x exposure time x transfer co-efficient /1000 x Body weight (70 kg). Where DFR = 20% of application rate for agricultural crops, 5% of application rate for turfgrass; exposure time was 8 hours.

Note: Hand harvesting for agricultural crops, except for turfgrass, is not shown here because PHIs are between 35 and 365 days. Therefore, DFR would be low by the time the crops are harvested. Hand weeding and/or mechanical weeding was also not shown since fenoxaprop-P-ethyl is a herbicide and can tank mixed with certain other herbicides. Therefore, it is unlikely that hand weeding and/or mechanical weeding will be conducted shortly after the application of fenoxaprop-P-ethyl.

Table 4 Occupational Postapplication Cancer Risk Estimates

Crop	Application rate (g a.i./ha)	Re-entry activity	Total Absorbed Daily Dose[a] (mg/kg bw/day)	Lifetime Average Daily Dose[b] (mg/kg bw/day)	Cancer Risk[c]	REI[d] (days)
Wheat, barley	92	Irrigation, scouting	3.91E-03	1.71E-04	1E-05	0
Rapeseed, canola, tame buckwheat, tame mustard, lentils	89	Irrigating, Scouting	3.79E-03	1.66E-04	1E-05	0
Peas, beans	89	Irrigating, Scouting	3.79E-03	1.66E-04	1E-05	0
Flax	101	Scouting	4.31E-03	1.89E-04	2E-05	2
Broccoli, cabbage, cauliflower	101	Thinning, scouting, irrigation	5.74E-03	2.52E-04	2E-05	4
Onion (dry bulb)	101	Irrigation, scouting, thinning	8.59E-04	3.76E-05	3E-06	0
Sunflower	101	Scouting	2.86E-03	1.25E-04	1E-05	0
Asparagus	54	Irrigation, scouting	7.66E-04	3.35E-05	3E-06	0
Carrots	54	Irrigation, scouting	4.59E-04	2.01E-05	2E-06	0
Soybeans	54	Irrigation, scouting	2.30E-03	1.01E-04	9E-05	0
Tomato	54	Staking, thinning, training, tying	1.53E-03	6.70E-05	6E-06	0
		Irrigation, scouting	1.07E-03	4.69E-05	4E-06	0
Potatoes	101	Irrigation, scouting	2.86E-03	1.25E-04	1E-05	0
Seedling alfalfa, red clover, alsike clover, white clover, sweet clover, sainfoin, bird's foot trefoil, cicer milkvetch for seed and forage	101	Irrigation, scouting	2.86E-03	1.25E-04	1E-05	0
Ryegrass, growing for seed	92	Irrigation, scouting	3.91E-03	1.71E-04	1E-05	0
Turfgrass, sod farms, golf courses	92	Harvesting, mowing, transplanting	4.87E-03	2.13E-04	2E-05	3
		Scouting, irrigation, fertilizing, aerating, hand pruning, seeding treated turf	3.54E-05	2.30E-06	2E-07	0

[a] ADD= daily dermal dose.
Dermal absorption = 40%.

[b] LADD = ADD x treatment frequency x working duration / (365 days/year x life expectancy (75 years)).
Where treatment frequency = 30 days for both agricultural and golf course workers. Working duration = 40 years (NAFTA, 1999).

[c] A Q_1* value of 0.087 (mg/kg/day) was considered appropriate to use in the cancer risk assessment.

[d] Day at which the cancer risk $\leq 1 \times 10^{-5}$.

Note: Hand harvesting for agricultural crops, except for turfgrass, is not shown here because PHIs are between 35 and 365 days. Therefore, DFR would be low by the time the crops are harvested. Hand weeding and/or mechanical weeding was also not shown since fenoxaprop-P-ethyl is a herbicide and can tank mixed with certain other herbicides. Therefore, it is unlikely that hand weeding and/or mechanical weeding will be conducted shortly after the application of fenoxaprop-P-ethyl.

Table 5 Residential Postapplication Non-Cancer Risk Estimate (at Day 0)

Crop	Re-entry activity	Application rate (µg/cm^2)	Dislodgeable residue value (µg/cm^2)[a]	Transfer coefficient for dermal contact[b] (cm^2/hour)	Exposure (mg/kg bw/day)				MOE	
					Dermal[c]	Hand-to-mouth[d]	Object-to mouth[e]	Soil ingestion[f]	Target= 300 (Adult)	Target=100 (Children)
Turfgrass, recreational areas and residential lawns	Adult, recreational	92 (2 applications, 21 day interval). 10% dissipation per day	0.051	14500	0.00845	n/a	n/a	n/a	1183	n/a
	Young, recreational		0.051	9986	0.0104515	n/a	n/a	n/a	n/a	144
	Toddler, recreational		0.051	5200	0.0141	0.00136	0.00017[g]	0.00000411	n/a	96
	Youth, golf course		0.051	344	0.0007199	n/a	n/a	n/a	n/a	2084
	Adult, golf course		0.051	500	0.00005828	n/a	n/a	n/a	171821	n/a

[a] 5% of application rate; a maximum of 2 applications per year with 21 day interval; 10% dissipation per day.
[b] Based on US EPA Policy 12, Standard Operating Procedures (SOPs) for Residential Exposure Assessments, revised February 22, 2001.
[c] Calculated as DFR x dermal absorption x exposure time x transfer co-efficient / 1000 x body weight (adult, 70 kg, 39 kg youth, child 15 kg).
[d] Toddler hand-to-mouth exposure was calculated as per US EPA Policy 12, Standard Operating Procedures (SOPs) for Residential Exposure Assessments, revised February 22, 2001): Hand-to-mouth Exposure = DFR x SA x Hand-to-mouth events x SEF x Duration / BW. SA: Surface area of a child's hand is 20cm^2 (USEPA, 2001); Hand-to-mouth events: Assumed 20 events/hour with 100% reloading of the hands between each event (USEPA 2001); SEF: Salia extraction factor, assumed 50% (USEPA, 2001); BW: 15 kg for children.
[e] Toddler object-to-mouth exposure was calculated as per US EPA Policy 12, Standard Operating Procedures (SOPs) for Residential Exposure Assessments, revised February 22, 2001): Object-to-mouth Exposure = DFR x Area of object x SEF / BW. Area of Object: A surface area of 25cm^2 represents the approximate area from which a child may grasp a handful or grass or "mouth" an object (USEPA, 2001); SEF: Salia extraction factor, assumed 50% (USEPA, 2001); BW: 15 kg for children.
[f] Toddler soil ingestion exposure was calculated as per US EPA Policy 12, Standard Operating Procedures (SOPs) for Residential Exposure Assessments, revised February 22, 2001): Soil ingestion = Application rate x IR_s x F x CF / BW. IR_s: 0.1 g US EPA SOPs 1997); F: Fraction of ai available in uppermost 1 cm of soil, 100% per cm soil; CF: 0.67cm^3/ g soil; BW: 15 kg for children.
[g] 20% of application rate.
Exposure time of 2 hours for recreation, and 4 hours for playing golf.

Table 6 Residential Postapplication Cancer Risk Estimate (at Day 0)

Crop	Application rate (g a.i./ha)	Re-entry activity	Absorbed Daily Dose[a] (mg/kg bw/day)	Lifetime Average Daily Dose[b] (mg/kg bw/day)	Cancer Risk[c]
Turfgrass, recreational areas and residential lawns	92 (2 applications, 21 day interval). 10% dissipation per day	Adult (recreational)	4.47E-03	1.44E-04	2E-0./5
		Youth (residential)	5.53E-03	1.70E-05	
		Toddler (recreational)	8.31E-03	2.55E-05	
		Youth (golf course)	3.81E-04	1.17E-06	2E-07
		Adult (golf course)	3.09E-05	9.94E-07	

[a] Absorbed Daily Dose = daily dose.
[b] LADD = ADD x Number of Days of Exposure x Duration of exposure / (365 days x Life expectancy). Number of Days of Exposure = 14 days; Duration of Exposure: 6 years for toddlers and youth, 63 years for adults; Life expectancy: 75 years
[c] A Q_1* value of 0.087 (mg/kg/day) was considered appropriate to use in the cancer risk assessment.

Table 7 Aggregate non-cancer Risk Estimate

Population Subgroup	Exposure route (mg/kg bw/day)	Exposure[a] (mg/kg bw/day)	MOE[b] (Target = 100)
Youth	Food and water	0.000007	550
	Residential exposure (golf)	0.0007199	
Adults	Food and water	0.000004	6431
	Residential exposure (golf)	0.00005828	

[a] Food and Water Exposure: 2005 PMRA review. Residential Exposure: Table 5 of Appendix IV.
[b] A NOAEL of 0.004 mg/kg bw/day was used calculated MOE

Table 8 Aggregate cancer Risk Estimate

Population Subgroup	Exposure route (mg/kg bw day)	Exposure route[a] (mg/kg bw day)	Cancer Risk[b]
Youth	Food and water	0.000007	7E-07
	Residential exposure (golf)	0.00000117	
Adults	Food and water	0.000005	5E-07
	Residential exposure (golf)	0.000000994	

[a] Food and Water Exposure: 2005 PMRA review. Residential Exposure: Table 5 of Appendix IV.
[b] A Q_1* value of 0.087 (mg/kg/day) was considered appropriate to use in the cancer risk assessment.

Appendix V Label Amendments for Products Containing Fenoxaprop-P-ethyl

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

A. For all end use products

I) The following statements must be included in a section entitled **PRECAUTIONS**.

Gloves must be worn during mixing and loading

II) The following statements must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

Toxic to aquatic organisms. To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay. Avoid application when heavy rain is forecast. Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body. As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pest. DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

B. For end use products registered for uses on potatoes, lentils, flax, sunflower, feed and forage crops, the following statement must be included in a section entitled **DIRECTIONS FOR USE**.

Limit custom mixer/loader/applicators to approximately 22 kg a.i./day or to 220 ha/day at the application rate of 101 g a.i./ha

C. For end use products registered for uses on flax, broccoli, cabbage and cauliflowers, the following REIs must be included in a section entitled **DIRECTIONS FOR USE**:

Crop	Activity	REI (days)
Flax	Scouting	2
Broccoli, cabbage, cauliflower	Thinning, scouting, irrigation	4

D. For end use products registered for uses on turfgrass

I) The following REI must be included in a section entitled **DIRECTIONS FOR USE:**

Crop	Activity	REI (days)
Turfgrass, sod farms and golf courses	harvesting, mowing, transplanting	3

II) The following statements must be included in a section entitled **DIRECTIONS FOR USE**:

DO NOT apply on recreational areas and residential lawns
DO NOT apply by high pressure handwand

E. For end use products registered for uses on barley and wheat, the following buffer zones must be included in a section entitled **DIRECTIONS FOR USE:**

Method of application	Buffer zone (metres) required	
	Aquatic Habitat	Terrestrial Habitat
Field Spray	0	1
Aerial	0	20

References

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B. LIST OF ADDITIONAL INFORMATION CONSIDERED (Published)

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Studies Considered in the Environmental Risk Assessment

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT (Unpublished)

PMRA#	Reference
659287	Final Study Report: Ecotoxicological evaluation of Puma120 Super, Aquatic plant (*Lemna gibba*) toxicity.
659288	Final Study Report: Ecotoxicological evaluation of Puma120 Super, Terrestrial plant seedling emergence.
659289	Final Study Report: Ecotoxicological evaluation of Puma120 Super, Terrestrial plant vegetative vigour.
659290	Buffer zone determination for the aerial application of Puma120 Super in Western Canada.