Proposed Re-evaluation Decision PRVD2011-06

MCPB

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Overview

Proposed Re-evaluation Decision for MCPB

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

An evaluation of available scientific information found that, under the proposed conditions of use:

- Most uses of MCPB products have value in the food and crop industry and do not pose unacceptable risks to human health or the environment. As a condition of the continued registration for these particular MCPB uses, new risk-reduction measures must be included on the labels of MCPB products. In addition, registrants must submit additional confirmatory scientific information identified in this document.

- Use of MCPB on dry/field peas and aerial application are proposed for phase out because the human health risks do not meet current standards.

- The application rate of 1.751 kg a.i/ha, which is used exclusively on peas, is no longer supported by the registrant and thus will be discontinued.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment.

This proposal affects all end-use products containing MCPB registered in Canada. Once the final re-evaluation decision is made, 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 MCPB 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.

This consultation document is presented in two parts. This Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessment of MCPB. A full copy of the Science Evaluation section is available upon request through Publications.

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

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation 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 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 conditions or proposed conditions of registration[2]. The Act also requires that products have value[3] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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

Before making a re-evaluation decision on MCPB, the PMRA will consider all comments received from the public in response to this consultation document[4]. The PMRA will then publish a Re-evaluation Decision document[5] on MCPB, which will include the decision, the reasons for it, a summary of comments received on the proposed 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 section.

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

3 "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".

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

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

What is MCPB?

MCPB is a selective systemic herbicide. It is registered for the post-emergence control of annual and perennial broadleaf weeds in terrestrial food crops, terrestrial feed crops and industrial oil seed crops and fibre crops. The rate of application for MCPB ranges from 1.031 to 1.594 kg a.i./ha. It is applied once per year. MCPB can be applied by ground and/or aerial equipment.

Health Considerations

Can Approved Uses of MCPB Affect Human Health?

MCPB is unlikely to affect human health when used according to revised label directions.

Potential exposure to MCPB may occur through diet or when handling and/or applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur in animal testing 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, pregnant women, nursing mothers and children). Only the uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose at which 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 products containing MCPB are used according to label directions.

MCPB is of moderate acute oral toxicity, low acute dermal toxicity, and slight acute inhalation toxicity in laboratory animals. MCPB is non-irritating to the skin, moderately irritating to the eyes and is not a dermal sensitizer.

The most sensitive endpoint for non-pregnant animals from the oral route of exposure is kidney toxicity. Test data indicated that MCPB is not likely to be carcinogenic or mutagenic in humans.

When MCPB is administered to pregnant rats and rabbits, reduced skeletal ossification and increased incidences of cranio-facial malformations are observed. Due to the nature of the effects and their potential implications on the health and survival of the fetus, extra protective factors are applied during the risk assessment to further reduce the allowable level of human exposure to MCPB.

With the proposed mitigation measures, the risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occur in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake (ADI) is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is expected to have no significant harmful effects.

Dietary exposure to MCPB was estimated from residues in treated crops and drinking water for different subpopulations representing different ages, genders and reproductive status. Acute and chronic exposure estimates were determined for the general population and all subpopulations including females of child-bearing age (13 to 49 years old), infants and children.

The aggregate acute exposure (i.e. to MCPB from food and drinking water) represents 39% of the acute reference dose for females 13 to 49 years old and is in the range of 1to 5% of the acute reference dose for all the other population subgroups when using drinking water concentrations generated from water modelling. The aggregate chronic exposure represents 5% of the chronic reference dose for the general population and is in the range of 4 to-10% of the chronic reference dose for all subpopulations. Thus, acute and chronic dietary risks are not of concern.

The *Food and Drugs Act* prohibits the sale of adulterated food; that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act.* Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that is at or below the established MRL does not pose an unacceptable health risk.

MRLs in/on all commodities treated with MCPB are currently regulated under B.15.002(1) of the Food and Drug Regulations which requires that residues do not exceed 0.1 ppm. Details regarding MRLs for MCPB can be found in the Science Evaluation Section.

Risks in Residential and Other Non-Occupational Environments

Residential and other non-occupational risks are not of concern.

MCPB is not registered for use in residential areas. Therefore, a non-occupational risk assessment was not required.

Occupational Risks from Handling MCPB

Occupational risks for handlers are not of concern with most crops provided that risk mitigation measures are applied. Occupational risks for handlers of MCPB for dry/field peas are of concern even with consideration of feasible risk mitigation measures. All aerial application scenarios are of concern with MCPB.

Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, the risk assessment of mixing/loading and application activities indicate that target margins of exposure (MOEs) are achieved for most crops provided that risk mitigation measures are applied. The MOEs for mixing/loading and application reach target MOEs for pastures, cereals (wheat, oats, barley and rye), seedling alfalfa, seedling clover, field corn, seedling grasses, and succulent/processing peas with the addition of mitigation measures including the use of additional protective equipment, engineering controls, and limiting the amount of kilograms handled per day.

Occupational post-application risks are not of concern for all crops provided that risk mitigation measures are applied.

Occupational post-application risk assessments consider exposure to workers entering treated agricultural sites. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, post-application risks to workers meet current standards and are not of concern for all crops provided that restricted entry intervals (REIs) are modified accordingly on the "use directions" (12 hours to 1 day) for most crops. For field corn, REIs were 15 and 23 days, depending on the activity. These REIs are considered to be agronomically feasible due to the timing of application. Consultation with user groups on the acceptability of these health protective use conditions is sought.

Environmental Considerations

What Happens When MCPB is Introduced Into the Environment?

MCPB poses a risk to terrestrial broadleaf plants, birds, small wild mammals and aquatic organisms including macrophyte plants and amphibians; therefore, additional risk-reduction measures need to be observed.

MCPB can enter non-target terrestrial habitats by drift from aerial or ground application such as pasture use, and it can enter aquatic habitats by run-off and leaching. It is water soluble and can move through the soil profile horizontally and vertically, thereby contaminating ground water and surface water, including drinking water sources. MCPB does not accumulate or bioconcentrate in the environment, and it is not persistent in soil, having a degradation half-life of 8.3 days depending on the type of soil. In aquatic environments, biotransformation eliminates fifty percent of the chemical in less than 18 days, and degradation by sunlight in surface water can be even more rapid.

Because of the specific mode of action affecting broadleaf plants (MCPB is a synthetic auxin plant hormone similar to other phenoxy herbicides such as 2,4-D), it is highly toxic to terrestrial plants such as trees, shrubs, crops and others. Non-target invertebrates including bees and beneficial insects are not likely to be affected by this chemical. Although vertebrate animals including birds and small wild mammals are not usually affected by MCPB's specific mode of action, some species show slight to moderate toxicity for oral/dietary exposure. In aquatic habitats, fish and invertebrates are not likely to be affected by MCPB based on available data, however, aquatic plants such as duck weed are sensitive.

The use of MCPB poses a risk to terrestrial and aquatic organisms, including plants, birds, mammals, aquatic plants and amphibians. To reduce exposure of terrestrial organisms, environmental hazard label statements are recommended. Terrestrial plants including crops and non-target plant habitats such as shelter belts and riparian zones along streams and ponds can be protected from adverse effects by the observance of specified spray restrictions which provide a spray buffer zone between sites of the application and non-target areas. Furthermore, precautionary label statements will be used to help reduce the potential for surface runoff and for ground water contamination.

Value Considerations

What is the Value of MCPB?

MCPB continues to contribute to weed management in a variety of crops when used in accordance with the label directions.

MCPB is one of the few post-emergent herbicides that controls a broad spectrum of annual and perennial broadleaf weeds in peas (dry/field and succulent/processing). MCPB is co-formulated with MCPA to broaden the spectrum of weed control. When formulated with MCPA, it is the only alternative to 2,4-DB registered for use in seedling clovers (wild white, Dutch white, ladino, alsike, and red clovers) alone or with a companion crop (wheat, barley and oats). It is one of the few post-emergent herbicides for use in seedling grasses and in seedling alfalfa grown for seed production. MCPB also plays a role in mitigating resistance development in weeds to other herbicide groups when used in rotation with them.

Measures to Minimize Risk

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

Risk-reduction measures are being proposed to address potential risks identified in this assessment. These measures, in addition to those already identified on existing MCPB product labels, are designed to further protect human health and the environment. The following additional key risk-reduction measures are being proposed.

Additional Key Risk-Reduction Measures

Human Health

- Phase out of aerial application on cereals and pastures and use on dry/field peas.
- Statements reducing dietary exposure:
    - When used on barley, oats, rye, wheat, field corn, peas (succulent/processing), pastures, and seedling grasses:
        - Do not permit lactating dairy animals to graze fields within 7 days after application;
        - Do not harvest forage or cut hay within 7 days after application;
        - Withdraw meat animals from treated fields at least 3 days before slaughter.
    - When used on seedling clover:
        - Do not permit lactating dairy animals to graze fields within 30 days after application;
        - Do not harvest forage or cut hay within 30 days after application;
        - Withdraw meat animals from treated fields at least 3 days before slaughter.
    - A minimum rotational crop plant back interval (PBI) of 12 months must be observed for all crops other than those registered for use with MCPA or MCPB.
- To protect workers entering treated fields, the following REIs are required:
    - Pastures: 1 day
    - Cereals: 1 day
    - Seedling alfalfa: 12 hours
    - Seedling clover: 1 day
    - Seedling grasses: 12 hours
    - Field corn: 15 days (scouting), 23 days (irrigation)
    - Peas (succulent/processing): 1 day
- Precautionary statements to avoid drift to areas of human habitation or areas of human activity.
- Additional personal protective equipment:
    - Coveralls over a long-sleeved shirt, long pants, and chemical-resistant gloves (no gloves required for groundboom application).
- Engineering controls:
    - Closed cab for groundboom application.
    - Closed mixing and loading (i.e. closed pump transfer system). The system must be capable of removing the product from the shipping container and transferring it into mixing tanks and/or application equipment.
- Limiting the amount of kg of a.i. handled per day:
    - Groundboom application: 111 kg a.i./day
        - For all crops, this limit equates to 70 ha at a maximum rate of 1.594 kg a.i./ha or area treated proportionally adjusted according to the specified label rate for the particular crop.
        - For seedling grasses, this limit equates to 85 ha at maximum rate of 1.313 kg a.i./ha or area treated proportionally adjusted according to the specified label rate for this crop.

Environment

- To reduce release of MCPB into the environment: changes to label statements include measures to reduce spray drift to non-target habitats, and to prevent unintentional contamination of such areas. Also to provide measures to reduce contamination of non-target sites resulting from surface runoff and leaching.
- To protect aquatic habitats: the inclusion of spray buffer zones on the label; i.e. the end-use products may not be sprayed within 1 to 175 metres of aquatic or terrestrial habitats. The specific distance depends on the type of spray equipment and the application rate.

What Additional Information is Being Requested?

Although the risks and value have been found to be acceptable when all risk-reduction measures are followed, with the exception of some uses, additional information is being requested from registrants and other stakeholders as a result of this re-evaluation:

Recent analytical data from at least five batches of the technical grade active ingredient (TGAI) must be provided 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: 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.

As a result of the proposed restrictions on the amount of MCPB handled per day as well as the proposed REIs, the PMRA is requesting feedback on:

- The acceptability of the proposed REIs for field corn at 15 days (scouting) and 23 days (irrigation) which are considered to be agronomically feasible due to the timing of application (refer to Section 3.2.2.2 and Appendix IV, Table 2 of the Science Evaluation);
- The feasibility of restricting the maximum amount of MCPB handled per day to 111 kg a.i./day, for seedling grasses, which corresponds to treating 85 ha/day.

Due to the proposed phase out of dry/field peas and aerial application, the PMRA is requesting feedback on:

- Extent of aerial application of MCPB in cereals and pastures;
- Potential impact of the proposed phase out of the use on dry/field peas and of aerial application of MCPB in cereals and pastures;

- Availability, viability and extent of use of alternative active ingredients registered for use on dry/field peas and aerial application on cereals and pastures;
- Availability, effectiveness and extent of use of non-chemical weed management practices in cereals and pastures and on dry/field peas.

Next Steps

Before making a re-evaluation decision on MCPB, 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 Document, which 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. At this time, information to confirm or refine the risk assessment will also be required (see Section 8.2 of the Science Evaluation).

Other Information

The test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

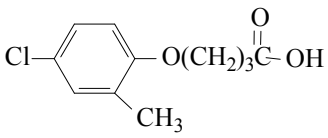
1.0 Introduction

MCPB is a selective systemic broadleaf weed herbicide. It belongs to the phenoxy acid family and is classified as a Group 4 herbicide. This herbicide produces an "auxin" overload, thereby causing susceptible broadleaf weeds to be controlled. It mimics the natural plant hormone indole-3-acetic acid (also known as auxin).

Following the re-evaluation announcement for MCPB, A.H. Marks and Company Limited (currently owned by Nufarm UK Ltd.) and Nufarm Agriculture Inc., the two registrants of the technical grade active ingredient (TGAI) and primary data providers in Canada, indicated that they intended to continue to support all uses included on the label of Commercial Class end-use products (EPs). There are no Domestic Class EPs containing MCPB registered in Canada.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	MCPB
Function	Herbicide
Chemical family	Phenoxycarboxylic acid
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	4-(4-chloro-o-tolyloxy)butyric acid
2. Chemical Abstracts Service (CAS)	4-(4-chloro-2-methylphenoxy)butanoic acid
CAS Registry Number	94-81-5
Molecular formula	$C_{11}H_{13}ClO_3$
Molecular weight	228.7
Structural formula	

Registration Number	Purity of the Technical Grade Active Ingredient
21808	95.5% nominal (limits: 92.5-98.5%)
27542	97% nominal (limits: 94-99%)

Identity of relevant impurities of human health or environmental concern
Both sources were analysed for the presence of tetra to hepta chlorinated dioxins and furans. Due to the recent re-evaluation decision on 2,4-D, the limit of dectection (LOD) used by the 2,4-D Task Force in the analysis of the same dioxins and furans was considered as a reference. With respect to MCPB, no dioxins or furans were detected at the specified LOD. However, a new analysis will be required to be consistent with current standards of LOD and limit of quantitation (LOQ) for these microcontaminants.

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 of the Technical Grade Active Ingredient

Property	Result	Interpretation
Vapour pressure at 25°C	9.83 x 10^{-2} mPa	Low volatility
Ultraviolet (UV)/visible spectrum	Not expected to absorb at $\lambda > 300$ nm.	Low potential to photodegrade in the environment.
Solubility in water at 20°C	pH / Solubility (g/L) 5 / 0.11 7 / 4.4 9 / 444	e.g. Soluble at neutral and acidic pHs but very soluble at alkaline pHs
n-Octanol/water partition coefficient (log Kow)	pH / Log K_{ow} 5 / >2.37 7 / 1.32 9 / -0.17	e.g. Not expected to bioconcentrate in natural waters
Dissociation constant (pKa)	pKa= 4.84	Weak acid, mobile at normal pH

2.3 Description of Registered MCPB Uses

Appendix I lists all MCPB products that are registered under the authority of the *Pest Control Products Act*, specifically including two TGAIs, one manufacturing concentrate and five Commercial Class end-use products (EP).

Appendix II lists all the uses for which MCPB is presently registered. All uses were supported by the registrants at the time of initiation of re-evaluation and were, therefore, considered in the health and environmental risk assessments. Also presented is whether any of the uses were added through the Pest Management Regulatory Agency (PMRA) Minor Use Program. While currently supported by the registrant, the data supporting these minor uses was originally generated by a user group.

Uses of MCPB belong to the following use site categories: terrestrial food crops, terrestrial feed crops and industrial oil seed crops and fibre crops. The crops specifically include cereal crops (wheat, oats, barley and rye), peas (dry/field and succulent/processing), pastures, field corn, seedling grasses and seedling clover (wild white, Dutch white, ladino, alsike, and red clovers) alone or with a companion crop (wheat, oats, and barley). MCPB is also registered as a User Requested Minor Use Label Expansion (URMULE) on seedling alfalfa grown for seed production in Western Canada only.

3.0 Impact on Human and Animal Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where 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. The health effects noted here were observed in animals at dose levels at least 100-fold (often much higher) above levels to which humans are normally exposed through use of products containing this chemical.

3.1 Toxicological Summary

MCPB is a chlorophenoxy herbicide that is structurally similar to MCPA; a herbicide of the same chemical class (PRVD 2007-01). Initially registered in 1956, available studies were conducted over a time span ranging from 1969 to 2007, with the majority of studies performed in the 1990s and 2000s. The toxicology database for MCPB combines chemical specific studies and MCPA studies which are used where MCPB is lacking with respect to the Pest Management Regulatory Agency's mandated data requirements and/or as supplementary data. The combined database is extensive including the standard battery of assays, as well as carcinogenicity, genotoxicity, developmental toxicity and mechanistic data. Published studies are also incorporated into the risk assessment. Overall, study results are consistent and indicate that the kidney is the target organ in the various animal species used in testing.

In orally dosed rats, MCPB is rapidly and extensively absorbed via the gastrointestinal tract. Excretion of MCPB is also rapid, with the majority of the administered dose eliminated within the first 48 hours. Excretion occurs primarily via the urine while a small amount is excreted in the feces. Urinary excretion did not increase proportionally at higher doses, instead, excretion in the feces increased, which indicates possible saturation of excretion processes and/or systemic absorption at higher doses. The proportion of MCPB recovered from body tissues is very low (< 3.6%), thus the potential for bioaccumulation is expected to be low.

Out of the 30 metabolites identified in rats, MCPA and HMCPA are the primary metabolites. MCPA is formed through β-oxidation, and is excreted primarily in urine. HMCPA is formed through the methyl hydroxylation of MCPA and is detected at lower levels in urine (5-9%) relative to MCPA (35-39%).

In rats or rabbits, MCPB was of moderate acute toxicity via the oral route, low toxicity via the dermal route, and slight toxicity via the inhalation route of exposure. MCPB was moderately irritating to the eyes of rabbits, non-irritating to their skin and was not a skin sensitizer when tested in guinea pigs.

In MCPB and MCPA repeat-dose dietary studies in the rat and dog, the dog appears to be the more sensitive species with kidney effects (increased creatine levels) observed at relatively low doses. Dogs have been found to be more sensitive to chlorophenoxy herbicides due to reduced clearance of organic acids compared to humans and rats and are therefore not relevant to human risk assessment (Timchalk, 2003; USEPA, 2005). In rats exposed orally to MCPB, the first treatment-related effect was increased alkaline phosphatase levels in females. At higher doses, increased kidney weight relative to brain weight, and decreased body weight gain and food consumption were also observed.

Short-term dermal toxicity was evaluated in rabbits using MCPA. Dermal toxicity was observed at 100 mg/kg bw/day (erythema, desquamation, and diffuse acanthosis) and kidney toxicity (renal tubule mineralization), decreased body weight gain, and hyperkeratosis was observed at 1000 mg/kg bw/day. A repeat-dose inhalation study is not available for MCPB or MCPA. No gender sensitivity is indicated by the available repeat-dose studies.

Potential effects from chronic exposure to MCPB were characterized on the basis of a two year dietary mouse oncogenicity study and a two year dietary rat chronic/oncogenicity study, both using MCPA. Effects from the mouse study were relatively mild at the lowest observed effect level, with increased kidney weight and kidney tubule casts observed in the high dose. In the rat study, decreased triglyceride levels at the mid-dose in males were not considered to be adverse, but may be an early indicator of potential hepatotoxicity. At higher doses, decreases in triglyceride levels and liver weight, and increased alanine aminotransferase confirmed earlier indications of hepatoxicity. Moderate nephropathy (renal toxicity) and iron storage in the spleen were also noted.

Neurotoxic effects were observed in acute and short-term MCPA rat studies. In the acute neurotoxicity studies, ataxia was observed consistently at most doses tested, while reduced open field activity and righting reflex, and increased abdominal tension was observed at higher doses. Three short-term neurotoxicity studies were performed using the acid, dimethyl amine salt, and the 2-ethylhexyl ester forms (2-EHE) of MCPA. In these studies, reduced motor activity was observed. MCPB has potential neurotoxic properties, and as such, the USEPA has requested a developmental neurotoxicity study to characterize pre- and post-natal neurotoxicity (USEPA, 2006). However, the conduct of this study has been reserved pending the completion and evaluation of the same study using MCPA. Although the PMRA has noted neurotoxic effects in

acute and subchronic neurotoxicity studies, these effects occurred only at very high doses, and are reversible in the acute studies.

The mutagenic potential of MCPB was assessed using a variety of bacterial and mammalian *in vitro* and *in vivo* studies. The overall weight-of-evidence suggests that MCPB is not genotoxic. Long-term studies with MCPA showed no evidence of carcinogenic potential.

Developmental toxicity studies conducted in rats and rabbits using MCPB or MCPA showed no evidence of teratogenicity at non-maternally toxic doses. Rabbits, however, are more sensitive than rats and rabbit fetuses displayed an increased incidence of cranio-facial malformations in the presence of severe maternal toxicity (mortality, reduced body weight, neuropathological effects, liver effects, kidney effects, and abortion). Although these malformations occur in the presence of serious maternal toxicity, there were no incidences reported in the study control or in the available historical control data (Middle Atlantic Reproduction and Teratology Association, 2009), and are therefore of concern. In a two-generation reproductive toxicity study using MCPA, there were no effects on fertility, gestation, or mating in any of the examined generations. A potential pup sensitivity was identified based on reduced body weight in the absence of maternal toxicity, however, two one-generation range finding studies showed no pup weight effects at doses higher than those tested in the two-generation reproductive toxicity study. Based on the weight of evidence provided by these three reproductive toxicity studies, there are no concerns for reproductive toxicity or sensitivity of the young animal.

Epidemiology

The PMRA identified one case-control study and two historical cohort studies exploring the potential health effects of MCPB, MCPA, and/or other phenoxy herbicide exposure in human populations. In the case-control study, Smith and Christophers (1992) sampled workers at a chemical production plant in Victoria, Australia and found no association between occupational exposure resulting from MCPB and/or MCPA production, and the development of soft tissue sarcomas and malignant lymphomas. A historical cohort study by Coggon et al. (1991) sampled workers from chemical manufacturers in Britain and found incidences of soft tissue sarcoma or lymphoma to be low based on the occupational exposure in workers studied. It was noted that the association of effects with specific chemicals was difficult due to the wide variety of chemicals produced at the factory. In the other historical cohort study, Saracci et al. (1991) interviewed production workers and sprayers exposed to chlorophenoxy herbicides and chlorinated phenols from 10 countries and found a statistically significant 6-fold increase in soft tissue sarcomas in workers 10-19 years after exposure, and a statistically significant 9-fold increase in sprayers. Because of the simultaneous exposure to various chlorophenoxy herbicides and chlorophenols, however, the study could not determine a specific chemical causing the increased incidences of soft tissue sarcomas.

Pest Control Products Act Hazard Consideration

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential pre- and post-natal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the exposure of and toxicity to infants and children, sufficient data are available for MCPB. The developmental/reproductive MCPB toxicity studies include one developmental toxicity study in rats and one in rabbits. There are also developmental toxicity studies for MCPA in rats (MCPA-acid, DMAS, 2-EHE) and rabbits (MCPA-acid) as well as a multi-generation reproduction study in rats (MCPA-acid). A developmental neurotoxicity (DNT) study is not included in the database, however, at this time, pre- and post-natal neurotoxicity is not of high concern. The noted neurotoxic effects in acute and subchronic neurotoxic studies with MCPA (and MCPA salts) occurred only at very high doses, and were reversible in the acute studies. The potential for MCPB developmental neurotoxicity is low.

In the rat two-generation reproduction study (MCPA), there is no concern for increased susceptibility of the offspring compared to parental animals even though the maximum tolerated dose was not achieved in the study. With respect to potential pre-natal toxicity, the developmental toxicity studies in rats and rabbits provided no strong indication of an increased susceptibility of fetuses to in utero exposure. In rats, effects on the fetuses (for example, reduced ossification) were only observed at a dose level that also resulted in toxicity in the dams. Rabbits showed maternal toxicity at lower levels than rats, which may reflect higher sensitivity via the oral route. In the rabbit developmental toxicity assay, effects including resorptions and cranio-facial malformations were observed in the presence of significant maternal toxicity, including mortality in some dams. Due to the seriousness of the effects, there is a high level of concern for the fetus, although this concern is tempered by the high degree of maternal toxicity. Therefore, the PCPA factor will be reduced to 3-fold for both acute and repeat exposure scenarios.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This 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. However, MOEs less than the target MOE require measures to mitigate (reduce) risk.

3.2.1 Toxicology Endpoint Selection for Occupational and Residential Risk Assessment

3.2.1.1 Short- and Intermediate-term Dermal Risk Assessment

For occupational short- and intermediate-term dermal risk assessment, an oral no observed adverse effect level of 5 mg/kg bw/day from a rabbit developmental toxicity study (MCPB) is used, based on effects on the developing fetus (cranio-facial malformations) in the presence of maternal toxicity at the lowest observed adverse effect level of 20 mg/kg bw/day (increased incidences of mortality, hypoactivity, paresis, paralysis, ataxia, loose feces, abortions, and reduced litters in the dams). A twenty one day dermal toxicity study in rabbits is available, but it did not include critical developmental endpoints.

The target **Margin of Exposure** for this study is **300**. A 10-fold factor was applied to account for interspecies extrapolation, as well as an additional 10-fold factor for intraspecies variability. As the worker population could include pregnant females, it was necessary to ensure adequate protection of the fetus that may be exposed via their mother. In light of concerns regarding pre-natal toxicity, an additional 3-fold factor was applied to these endpoints to protect for a sensitive subpopulation (namely women 13 – 49 years of age).

3.2.1.2 Short- and intermediate-term inhalation risk assessment

For occupational short- and intermediate-term inhalation risk assessment, the no observed adverse effect level of 5 mg/kg bw/day from a developmental toxicity study in the rabbit was selected based on effects on the developing fetus (cranio-facial malformations) in the presence of maternal toxicity. There were increased incidences of mortality, hypoactivity, paresis, paralysis, ataxia, loose feces, abortions, and reduced litters in the dams, and _owest ears and dilated lateral ventricle in the offspring at the lowest observed adverse effect level of 20 mg/kg bw/day.

The target **Margin of Exposure** for this study is **300**. A 10-fold factor was applied to account for interspecies extrapolation, as well as an additional 10-fold factor for intraspecies variability. As the worker population could include pregnant females, it was necessary to ensure adequate protection of the fetus that may be exposed via their mother. In light of concerns regarding pre-natal toxicity, an additional 3-fold factor was applied to these endpoints to protect for a sensitive subpopulation (namely women 13 – 49 years of age).

3.2.1.3 Long-term Dermal and Inhalation Risk Assessment

Based on the current use pattern for pest control products containing MCPB, long term dermal and inhalation exposure is not expected, thus, a long term dermal and inhalation risk assessment is not required.

3.2.1.4 Cancer Risk Assessment

The weight of evidence indicates no evidence for carcinogenicity for MCPB and therefore a cancer risk assessment is not required.

3.2.1.5 Dermal Absorption

One *in vivo* dermal absorption study (Beimborn and Leibold, 2003) was submitted and reviewed by PMRA. Four male rats/group were exposed to concentrations of 4 and 0.067 mg a.i./cm^2 for 4 or 10 hours and sacrificed after 4, 10, 24, and 96 hours to determine dermal absorption. Two values were considered for the dermal absorption estimate. The low dose group of the 10 hour exposure duration captured the likely worker exposure timeframe, leading to a mean total absorption value of 51% (including skin bound residues of 20%). Higher absorption values were detected in the high dose groups coinciding with a trend of increased dermal penetration that may be attributed to skin irritation/damage. The average dermal absorption in the high dose group was approximately 75% (including skin bound residues of 3% on average). To be protective of the mixer/loaders that handle the concentrated formulation which is represented by the high dose, a dermal absorption value of 75% was chosen for risk assessment purposes. Dermal absorption of 51% was selected for assessing risks for post-application workers that are exposed to lower concentrations. The duration of the study was not long enough to determine the fate of skin bound residues, although there was a clear trend that the skin bound residues were being absorbed during the study period. Therefore, the skin bound residues were included. Since there are minimal skin bound residues at the high dose (~3%), this value contributes minimally to the overall estimate of dermal absorption.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to MCPB through mixing, loading or applying the herbicide during normal use, and when entering a treated site to conduct activities such as scouting treated crops. A quantitative risk assessment was conducted to determine the amount of exposure.

3.2.2.1 Mixer, Loader and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders and applicators. The following supported uses were assessed:

- Mixing/loading of liquids or solutions
- Aerial application to cereal grains (wheat, barley, rye, oats) and pastures
- Groundboom application to field corn, seedling grasses, seedling clovers, seedling alfalfa, peas (dry/field and succulent/processing), pastures, cereal grains (wheat, barley, rye, oats)

Occupational handlers of MCPB include farmers and custom agricultural applicators who mix, load and apply the herbicide. As only one application is permitted per year, the duration of exposure for farmers is expected to be short-term (up to 30 days). In the case of custom applicators, the duration of exposure may be intermediate (1 – 6 months).

The PMRA estimated handler exposure based on different levels of personal protective equipment:

Baseline PPE: Long pants, long sleeved shirt and chemical-resistant gloves (unless specified otherwise). For both groundboom and aerial application, this scenario does not include gloves, as the data quality was better for non-gloved scenarios than gloved scenarios.

Mid-level PPE: Coveralls over a single layer (long pants and long sleeved shirt) and chemical-resistant gloves.

Maximum PPE: Chemical-resistant coveralls over a single layer (long pants and long sleeved shirt) and chemical-resistant gloves.

Engineering Controls: Closed cab application for groundboom with applicators wearing coveralls over a single layer (no gloves). Closed mixing and loading of liquids for groundboom application with workers wearing coveralls over a single layer and chemical-resistant gloves. Closed mixing and loading of liquids for aerial application with workers wearing chemical resistant coveralls over a single layer and chemical-resistant gloves.

No chemical-specific exposure studies were available for use in the re-evaluation of MCPB. Thus, appropriate exposures were estimated using the *Pesticide Handlers Exposure Database (PHED), Version 1.1*. PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment.

In most cases, PHED did not contain appropriate data sets to estimate exposure to workers wearing chemical resistant coveralls. As necessary, PHED unit exposures were adjusted by protection factors of 75% for coveralls, 90% for chemical resistant coveralls, and 90% for chemical resistant gloves.

Calculated MOEs are summarized in Table 1 of Appendix VI. Target MOEs are achieved for most crops provided that risk mitigation measures are used. Target MOEs are not reached for dry/field peas even with consideration of feasible mitigation measures and all aerial application scenarios are below the target MOE as well. Proposed mitigation measures are described in Section 8.0.

For seedling grasses, the calculated MOE of 250 did not reach the target of 300 based on an area treated per day of 100 hectares. However, a restriction on the amount handled of 111 kg a.i./day, which corresponds to approximately 85 hectares for this crop, would be considered acceptable to address the risk concern.

3.2.2.2 Post-application Worker Exposure and Risk Assessment

The post-application occupational risk assessment considers exposure to workers entering treated agricultural sites. Inhalation exposure is expected to be low due to the low vapour pressure of MCPB. Post-application exposure includes activities such as scouting and irrigation. Due to the fact that there is only one application per season, exposure is likely to be short-term in duration. Dermal exposure to workers entering treated areas is estimated using default dislodgeable foliar residue (DFR) values and transfer coefficients (TC), which are activity specific.

Activity-specific transfer coefficients reported in the *Science Advisory Council for Exposure Agricultural Transfer Coefficient* (Revised - August 7, 2000) were used in the assessment of post-application exposure. Agricultural crops were grouped together based on similar transfer coefficients and dislodgeable foliar residues.

Risk is managed by establishing a restricted entry interval (REI) for specific tasks. A REI is the duration of time which must elapse before residues decline to a level where entry into a treated area to perform a specific activity will result in a margin of exposure above the agency target.

Based on PMRA use information, the timing of MCPB application typically occurs during early stages of post-emergence plant growth. Therefore, it is appropriate to assume relatively low crop heights and minimum foliage for all crops except for field corn. For field corn, plants can reach up to 60 cm in height prior to application and thus TC values assuming high crop heights and full foliage were selected.

After one application of MCPB, the calculated REIs ranged from 12 hours to 1 day in all crops except for field corn which had REIs of 15 and 23 days for scouting and irrigation respectively. The REIs are considered to be agronomically feasible for scouting or irrigation activities of all crops.

3.2.3 Non-Occupational and Residential Exposure and Risk Assessment

3.2.3.1 Non-occupational Risk

MCPB is not registered for use in residential areas. Therefore, a residential assessment was not required.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to MCPB from potentially treated imported foods is also included in the assessment. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences

and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User's Guide*, presents detailed acute and chronic risk assessments procedures.

Residue estimates used in the dietary risk assessment (DRA) may be conservatively based on the maximum residue limits (MRLs) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (PDP).
Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.03), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994–1996 and 1998.

The assessments were performed by using MRL/tolerance-level residues assuming 100% crop treated (CT). As no MRLs are currently established on MCPB registered crops, the 0.1 ppm default MRL was used for all food commodities of plant origin according to B.15.002(1) of the Food and Drug Regulations. As no information on residue levels in animal commodities was available, 0.1 ppm was used based on assumptions made from MCPB metabolism studies and available feedstuff residue data for the pesticide, MCPA, as well as assuming total conversion of MCPB into MCPA in animals. Therefore, restrictive label statements are proposed with regard to pre-grazing intervals until MCPB (including its metabolite MCPA) residue data in grass and cereal feedstuffs (forage, straw, hay) are submitted to allow an adequate estimation of the magnitude of residue transferable to animal commodities. The following inputs were used also in the risk assessment: Dietary Exposure Evaluation Model (DEEM) default processing factors for all commodities and drinking water estimated environmental concentration (EEC) point estimates from water modelling.

In addition to the uncertainties related to the estimation of residues in animal commodities, the nature and magnitude of residues in secondary crops could not be determined as no confined rotational crop trial study was submitted. In order to minimize potential transfer of residues to secondary crops, restrictive label statements with regard to crop rotation are proposed as a result of this evaluation.

For more information on dietary risk estimates or residue chemistry information used in the dietary assessment as well as additional residue chemistry data gaps, see Appendices VII and VIII.

3.3.1 Determination of Acute Reference Dose

Acute Reference Dose, Females 13-49 Years of Age
For females of child-bearing age (13-49 years of age), a no observed adverse effect level of 5 mg/kg bw/day was selected from a developmental rabbit study (MCPB), based on effects on the developing fetus (cranio-facial malformations) in the presence of maternal toxicity at the lowest observed adverse effect level of 20 mg/kg bw/day. This effect was considered a relevant endpoint that could result from an acute exposure. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are applied. The PCPA factor is reduced to 3-fold to account for the seriousness of developmental effects on the developing rabbit fetus in the presence of maternal toxicity. The composite assessment factor is 300. The resulting acute reference dose (ARfD) is 0.017 mg/kg bw (5 mg/kg bw ÷ 300).

Acute Reference Dose, General Population (Excluding Females 13-49 Years of Age)
To estimate acute dietary risk (one day) for the general population, a lowest observed adverse effect level of 146 mg/kg bw was selected from an acute neurotoxicity study (MCPA-DMA salt) based on clinical signs of neurotoxicity (specifically, ataxia). Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are applied. A 3-fold uncertainty factor is applied based on the lack of a no observed adverse effect level (NOAEL). Overall, the database is adequate for determining post-natal toxicity, and pre-natal toxicity concerns have been addressed through a risk assessment specific to females aged 13-49. Accordingly, in exposure scenarios for children, the risk is considered well characterized and the PCPA factor is reduced to 1-fold. The composite assessment factor is 300. The resulting ARfD for the general population is 0.5 mg/kg bw (146 mg/kg bw ÷ 300).

3.3.2 Acute Dietary Exposure and Risk Assessment

The acute dietary risk was calculated considering the highest ingestion of MCPB that would be likely on any one day, and using food consumption and food residue values. The expected intake of residues is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is not of concern.

Acute aggregate (food + drinking water) dietary exposure assessments were performed for females 13-49 years of age (ARfD = 0.017 mg/kg bw) and all other population subgroups (ARfD = 0.5 mg/kg bw). The results show that the acute deterministic (at the 95th percentile) exposure estimate for females 13-49 years of age is not of concern, at about 39% of the ARfD. The main contributor to the risk is water (direct and indirect, all sources), accounting for about 95% of the total exposure (37% of the ARfD). The acute exposure estimates for the other population subgroups are in the range of 1-5% of the ARfD, and are not of concern. The most exposed population subgroup is infants less than 1 year old, at approximately 5% of the ARfD.

3.3.3 Determination of Acceptable Daily Intake

Acceptable Daily Intake – All Populations
To estimate dietary risk from repeat exposure, the rabbit developmental toxicity study was used. A NOAEL of 5 mg/kg bw/day was established based on effects on the developing fetus (cranio-facial malformations) in the presence of maternal toxicity at the lowest observed adverse effect level of 20 mg/kg bw/day. There was no strong evidence of increased sensitivity/susceptibility of fetuses of rats and rabbits dosed with MCPB during pregnancy (in utero exposure), and even though developmental neurotoxicity study was lacking, the remainder of studies were well conducted with defined NOAELs. The fetal effects observed in the rabbit developmental toxicity assay were considered serious endpoints although the concern was tempered by the presence of maternal toxicity. Therefore, the PCPA factor was reduced to 3-fold for repeat exposure scenarios for women of child bearing age. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability are used. The resulting acceptable daily intake (ADI) is 0.017 mg/kg bw/day (5 mg/kg bw/day ÷ 300). This reference dose was deemed protective for all other sub-populations.

3.3.4 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and the average residue values on those foods. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is not of concern.

Chronic aggregate (food + drinking water) dietary exposure assessments were performed for the general population including all population subgroups (ADI = 0.017 mg/kg/day). The results show that the chronic exposure estimate for the general population is not of concern, at about 5% of the ADI. Exposure estimates for all the population subgroups are in the range of 4-10% of the ADI and are also not of concern. The most exposed population subgroups are infants and children below 5 years of age. The main contributor to the risk for these subgroups is water (direct and indirect, all sources), accounting for about 70% and 30% of the total exposure (7% and 3% of the ADI) for all infants less than 1 year old and children 1 – 5 years old, respectively.

3.4 Exposure from Drinking Water

3.4.1 Concentrations in Drinking Water

Level 1 drinking water estimated environment concentrations (EECs) of combined residues of MCPB and its transformation product MCPA were calculated using PRZM/EXAMS and LEACHM models for surface and groundwater, respectively. The modelling was based on the maximum annual application rate for use on peas (dry/field and succulent/processing), wheat (spring and durum), barley, seedling clover and field corn, with 1 application of 1.594 kg a.i./ha per year. The highest (most conservative) surface water reservoir yearly peak EEC value of 0.127 ppm and the yearly average surface water dugout EEC value of 0.018 ppm are used in the acute and the chronic dietary risk assessments, respectively.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure estimates were not calculated separately. They were combined with food exposure estimates, with EEC point estimates incorporated directly in the dietary (food + drinking water) assessment. Please refer to Sections 3.3.2, 3.3.4 and 3.5 for details.

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation). As there are no residential or other non-occupational uses of MCPB the aggregate assessment consists of exposures from food and drinking water only (Sections 3.3 and 3.4).

3.6 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. Incidents are classified into six major categories including effects on humans, effects on domestic animals and packaging failure. Incidents are further classified by severity, in the case of humans for instance, from minor effects such as skin rash, headache, etc., to major effects such as reproductive or developmental effects, life-threatening conditions or death.

The PMRA will examine incident reports and, where there are reasonable grounds to suggest that the health and environmental risks of the pesticide are no longer acceptable, appropriate measures will be taken, ranging from minor label changes to discontinuation of the product. Incident reports reflect the observations and opinion of the person reporting it and the Incident Reporting Program does not include validation of the reports. The PMRA collects incident reports in an effort to establish trends and the publishing of individual reports should not be considered as a statement of causality.

As of January 25, 2010, there have been no health-related incident reports for MCPB in Canada.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Summary: Available fate data (Appendix IX, Table 6) indicate that MCPB is expected to be non-persistent in soil and slightly persistent in water. MCPB is very soluble in water and it is mobile in soil; thus, it is expected to leach to ground water. MCPB is unlikely to bioaccumulate due to a low K_{ow} value. Phototransformation is not an important route of dissipation on soil, whereas water phototransformation is rapid and behaves as an important route to transformation under certain conditions.

It should be noted that the application rate chosen to calculate the EECs at the screening level is a combination of the maximum application rate of 1.594 kg a.i./ha (MCPB) + 0.106 kg a.i./ha (MCPA) resulting in a total rate of 1.700 kg a.i./ha. This combined rate was chosen since four of the five registered formulations of MCPB also contained a small amount of MCPA which is also a registered herbicide active ingredient. MCPA is a transformation product of MCPB and has the same mode of action in plants. These two actives are assumed to have similar additive toxicity to non-target plants and other organisms; therefore, this combined application rate is used to determine the risk to non-target species.

Hydrolysis
Hydrolysis is not expected to be a transformation route for MCPB in aquatic systems as it is stable.

Phototransformation
Phototransformation of MCPB on soil is not an important route of transformation in the environment with a half-life ($t_{½}$) of 30 days. In surface waters, phototransformation is expected to be an important route of transformation ($t_{½}$ = 2.6 days at neutral pH) depending on latitude, weather, and water depth. Three major transformation products are produced at neutral pH by aquatic photolysis, namely; a) 4-(4-hydroxy-o-tolyloxy) butyric acid; b) 2,4-dihydroxyphenylformate; and, c) O-cresol.

Volatilization
A low vapour pressure (vp = 4 x 10^{-7} mm Hg) and a Henry's Law constant of 4 x 10^{-6} atm m^3/mol (1/H = 1.33 x 10^{-8}) suggest that volatilization from water is not likely to be a significant process contributing to the dissipation of MCPB from the aquatic environment. This can also be said for moist soil.

Soil Biotransformation
MCPB is transformed by microorganisms under both anaerobic and aerobic conditions. In aerobic soils, MCPB was found to have a dissipation time (DT_{50}) of 8 days which would classify MCPB as non-persistent. In anaerobic soils, MCPB is similarly non-persistent having a DT_{50} of 8.3 days. The only major transformation product identified in the available anaerobic soil transformation study was MCPA (46% of applied radioactivity), which was observed to be declining by the end of the study.

Soil Mobility
Calculated soil K_{oc}'s range from 31 – 129 and indicate that MCPB does not strongly sorb to soil and thus can potentially be mobile. On the basis of soil thin layer chromatography (TLC) studies, MCPB is classified as highly to very highly mobile (McCall et al., 1981), while in sediment it is moderately mobile (K_{oc} = 371). MCPB satisfies almost all of the criteria set out by Cohen et. al. (1984); therefore, there is a high potential for MCPB to leach in soils resulting in groundwater contamination. In addition, the calculated GUS score (Gustafson, 1989) is 1.92 based on the soil studies which classifies MCPB as a moderate leacher. Therefore, the PMRA concludes that MCPB has the potential to leach to groundwater which is supported by modelling estimates of 18 µg/L. MCPB's high solubility and soil mobility also indicate that it is likely to reach surface

water sources via runoff. Modelled surface water concentrations range up to 127 ug/L although detections in the field were below 1 ug/L.

Canadian Field Dissipation
No information is available on field dissipation of MCPB; however, rapid dissipation, including leaching, runoff and surface water recharge (under favourable conditions), is expected based on the available laboratory fate data. American field dissipation studies were required by the USEPA as part of their reregistration assessment of MCPB. When available, studies relevant to similar areas of use in Canada will be reviewed by the PMRA.

Aquatic Biotransformation
In water, aerobic biotransformation is the main route of transformation of MCPB ($t_{1/2}$ = 8.7-18 days in sediment water systems). This classifies MCPB as slightly persistent in water (McEwen and Stephenson, 1979). Due to the high solubility, low soil K_{oc}'s (31-129) and low log K_{ow} (1.36), MCPB is likely to be in solution form in aquatic environments rather than adsorbed/dissolved or suspended in organic matter. Hence, MCPB is available for biotransformation in the water column.

Surface Water Monitoring
A search for MCPB water monitoring data in Canada revealed that routine analysis for MCPB is not conducted as indicated by samples that were collected in areas where low to no use occurs. The rate of detection across provinces was low (<10%) as were detection levels and measured concentrations. For example, the highest mean concentration measured at any one location was 0.53 µg/L.

Transformation Products
MCPB undergoes transformation in soil and aquatic systems and produces no major transformation products other than MCPA (anaerobic soil and aerobic aquatic systems). Phototransformation in water produces three major transformation products as previously listed above.

4.2 Risk to Non-Target Species

The environmental risk assessment integrates 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 concentrations (EECs) are pesticide concentrations in various environmental media such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rates, chemical and environmental fate properties and the transformation 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 which identify those groups of organisms where 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 then the RQ is compared to the level of concern (LOC = 1). If the screening level RQ is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level RQ 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 until no further refinements are possible.

Refined Assessment

Birds, Mammals and Terrestrial Organisms

Given the conservative assumptions taken in the screening level assessment, and that the LOC was exceeded for some bird guilds, mammals and terrestrial plants, the risk was further characterized by taking into consideration off-field exposure that resulted from pesticide drift during application (Appendix IX, Table 8-2). For this assessment, the deposition rate (or the rate at which the non-target plants will be exposed) was determined by taking into consideration the percent drift that will result depending on the application method. A spray droplet size of 'medium', based on the American Society of Agricultural Engineers (ASAE) classification, can be assumed for herbicides applied by a field sprayer. For a 'medium' droplet size, the maximum spray drift deposition for a groundboom sprayer onto agricultural crops at a point one metre downwind from the point of application is equal to 6% of the application rate. Similarly for aerial application, off-site deposition rates for MCPB uses are 23% and 60% depending on crop use or non-crop use applications. Therefore, the maximum off-field deposition on bird and mammal food items and non-target plants would be: 0.102 kg a.i./ha (1.700 kg a.i./ha x 0.06) for ground applications and 0.391 kg a.i./ha to 1.020 kg a.i./ha for aerial applications. Additionally, RQs for birds and mammals were recalculated based on mean estimated daily exposure (EDE) for EDE nomogram values.

Runoff

For the Level 1 aquatic eco-scenario assessment, EECs of MCPB from runoff into a receiving water body were simulated using the PRZM/EXAMS models. The PRZM/EXAMS models simulate pesticide runoff from a treated field into an adjacent water body and the fate of the pesticide within that water body. At the Level 1 assessment, a water body consists of a 1 hectare wetland with an average depth of 0.8 metres and a drainage area of 10 hectares. A seasonal water body was also used to assess the risk to amphibians as a risk was identified at the screening level. This type of water body represents a scaled down version of the permanent water body

noted above, but having a water depth of 0.15 metres. In this case, this seasonal water body was used as a refinement to assess the risk to amphibians as their risk quotient was the highest.

Spray Drift
Similar to the terrestrial risk assessment, the risk to aquatic organisms from spray drift off a treated site was also assessed taking into consideration the spray drift deposition at a spray quality of ASAE 'medium' for groundboom (6%), aerial crop use (23%) and aerial non-crop use (60%) at 1 metre downwind from the site of application.

4.2.1 Risk to Terrestrial Organisms

A risk assessment of MCPB on terrestrial organisms was based upon an evaluation of toxicity data on bees (acute contact), earthworms (acute), two standard test species of birds (acute oral, dietary), rats (acute oral), and including terrestrial plants (vegetative vigour and seedling emergence). A summary of terrestrial toxicity data for MCPB is presented in Appendix XI, Table 7-1. For the assessment of risk, toxicity endpoints were chosen from the most sensitive species and used as surrogates for the wide range of species that can be potentially exposed following application of MCPB.

Invertebrates
The screening level risk assessment indicated that the level of concern for terrestrial invertebrates (e.g. bees, earthworms or beneficial insects) was not exceeded at any of the application rates. Appendix IX, Table 8-2 summarise the risk quotients for terrestrial invertebrates.

Birds and Small Wild Mammals
Standard exposure scenarios on vegetation and other food sources were based on correlations in Hoerger and Kenaga (1972), Kenaga (1973), and modified according to Fletcher *et al.* (1994). This information was used to determine the concentration of pesticide (dry weight) on various food items in the diet of birds and small wild mammals, or to determine estimated daily exposure (EDE). Exposure is dependent on the body weight of the organism and the amount and type of food consumed. In the screening level assessment, a set of generic body weights was used for birds (20, 100, and 1000g) and small wild mammals (15, 35, and 1000 g) to represent a range of bird and small wild mammal species. For each body weight, the food ingestion rate (FIR – equivalent to food consumption) was based on equations from Nagy (1987). It should be noted that diets of animals can be highly variable from season to season as well as day to day. Furthermore, animals are often opportunists and if they encounter an abundant and/or desirable food source, they may consume large quantities of that food. For these reasons, the screening level assessment used relevant food categories for each size group consisting of 100% of a particular dietary item. These items included the most conservative residue values for plants, grains/seeds, insects, and fruits. It should be noted that a diet of 100% plant material for smaller birds (i.e. 20 and 100 g) is not included in the determination of the EDE as this is considered unrealistic. Small birds in North America are not known to eat a diet primarily of leafy plant material or grass as a small bird would need to consume unrealistically high amounts of these

materials to meet its energy requirements. Similarly, a 100% diet of plants for the smallest size of mammal (15 g) is not included in the assessment.

Birds

Birds can be exposed to MCPB through the consumption of contaminated food (e.g. seeds, insects, and vegetation), drinking water and dermal contact; however the present assessment only considered food sources. MCPB can pose an acute risk to some feeding guilds of birds. Following one groundboom application of MCPB at 1.700 kg a.i./ha, the acute oral LOC is only exceeded by a factor of 1.7 for 20 gram fructivores and by a factor of 3.4 for insectivores that are feeding directly on the treated field. The corresponding risk for medium sized birds for the same feeding guilds was 1.3-2.6. For large birds (1000 g), the LOC was exceeded marginally for grasses, forage crops and leafy foliage with RQs of 1.7-5.1.

Acute dietary exposure to MCPB presents a risk to some birds feeding directly on the treated field with the LOC of 1 being exceeded. The acute dietary LOC is exceeded by a factor of 3.4 in small insectivores, by a factor of 1.4 in medium insectivores, and by a factor of 5.1 in large herbivores feeding on leafy foliage. Chronic data is not available; however, chronic risk is not expected in birds based on the rapid dissipation of MCPB under field conditions, a single allowable application per year, and available data on chronic effects of MCPA.

Based on the screening results, there is the potential for acute adverse effects in large herbivores feeding on leafy crops/plants based on the LOC being exceeded by up to 5.1 from dietary exposure to MCPB herbicide contaminated food items (based on the assumption that birds consume 100% treated diet). However, it is generally not expected that significant acute or chronic adverse effects would manifest for many species of birds under field conditions.

Refined Assessment

Using this approach, the assessment indicated that there are fewer bird guilds with LOCs > 1 and only one small mammal feeding guild where the LOC >1. The off field risk to birds from the use of MCPB herbicide is lower with RQs being less than 1.2 at 6-23% drift. At 60% drift and aerial non-crop applications for pastures at 1.700 kg a.i./ha, RQs range from 2 (for small sized insectivores) to 3.1 (for large herbivore birds). In order to refine the risk to birds, the PMRA may consider mean EDE exposures instead of the maximum nomogram values used in the screening assessment. Risk quotients to birds based on mean nomogram EDEs, instead of maximum values, range up to 1.9 for small insectivores feeding on treated fields while the off-field RQs (60% drift deposition) are all below 1.1. However, additional label statements concerning toxicity to birds are required.

Mammals

Mammals can be exposed to MCPB through consumption of contaminated food (e.g. vegetation, insects, and seeds) and through water and dermal uptake; however, only dietary exposure is considered in this assessment. The acute oral LOC is not exceeded for small mammals exposed to MCPB contaminated vegetation and is only exceeded by a factor of 1-3.2 for medium

herbivores following one groundboom application of 1.700 kg a.i./ha. Note that the corresponding value for mammals of a large size is 1.75.

Refined Assessment

Off field exposure resulting from up to 60% drift within 1 metre of an area treated aerially is expected to pose limited risk to small mammals based on the RQ exceeding the LOC by a factor of 1.9 for a single feeding guild (35 g herbivores). Based on mean EDE nomogram values (instead of maximum values used at the screening level), the RQ of 3.2 for medium sized herbivores feeding on a treated field becomes 1.0, thus indicating that the risk to mammals is unlikely to be of concern. However, additional label statements concerning toxicity to mammals are required.

Terrestrial Plants

Non-target terrestrial vascular plants could be exposed to residues of MCPB as a result of spray drift from the application of the associated end-use products. Seedling emergence and vegetative vigour studies on ten crop species were submitted. Using the endpoints from both study types and the maximum seasonal application rate, the screening level risk assessment indicated that level of concern was exceeded for terrestrial plants (RQ = 33-77) (Appendix IX, Table 8-2).

Refined Assessment

Based on the revised risk quotients using the off-field estimated environmental concentrations from drift, the level of concern for terrestrial vascular plants was still exceeded (RQ = 4.6 – 46). The use of MCPB containing herbicides is expected to pose risks to non-target terrestrial plants, thus, mitigation measures will be applied in the form of spray buffer zones and label statements. Tables 8-2 and 8-3 of Appendix IX summarize the risk assessment for MCPB for terrestrial organisms.

4.2.2 Effects on Aquatic Organisms

Risk to aquatic organisms is based on an evaluation of toxicity data on MCPB for eight freshwater species (one invertebrate, two fish, one macrophyte, and four algae) and one estuarine/marine species (diatom). A summary of aquatic toxicity data for MCPB is presented in Table 7-2 of Appendix IX. For the assessment of risk, toxicity endpoints chosen from the most sensitive species were used as surrogates for the wide range of species that can be potentially exposed following treatment with MCPB (Table 9-1). For the screening level scenario, expected environmental concentrations were determined based on the overspray of an 80 cm deep body of water for fish and invertebrate and a 15 cm depth was used to estimate the risk to amphibians. These water depths are also used in the refined assessments which characterize risk resulting from drift or runoff. It should be noted that chronic risk could not be assessed due to the lack of chronic toxicity data for aquatic organisms. MCPB is not expected to be persistent in aquatic systems near treated areas given that it has a $t_{1/2}$ of 9 – 18 days (based on the water/sediment dissipation rate) and that MCPB is only applied once per year. Given the above and taking into

consideration the mode of action of MCPB, it is expected that chronic exposure is unlikely to be of concern for most aquatic organisms.

Fish, Invertebrates and Amphibians
The screening level assessment for aquatic organisms indicates that the acute levels of concern were not exceeded for freshwater invertebrates or fish. The LOC was exceeded for amphibians for acute effects, although no amphibian data was available and effects were estimated from fish toxicity data (1/10 acute LC_{50}, RQ = 2.8) with a shallow water body depth of 15 cm. Given the fate characteristics of MCPB (i.e. short half-life) and a single application per season, amphibians are not expected to be at significant risk from exposure to MCPB under field use conditions.

Aquatic Plants
The screening level LOC was exceeded for duck weed (*Lemna* sp.) for acute effects from direct application of MCPB to a water body, with an RQ of 2. Algae are less sensitive than macrophytes and are not considered to be at significant risk from exposure to MCPB (RQ = 1.05).

Runoff Refinement
The highest peak value of 0.36 mg a.i./L was used for the acute risk assessment. The acute LOC was not exceeded for amphibians exposed to the peak MCPB concentration of 0.36 mg a.i./L in runoff (RQ = 0.92). Therefore, aquatic organisms would be at negligible risk from residues of MCPB in runoff following all applications in Canada (Tables 9-1 and 9-2).

Spray Drift Refinement
The acute LOC for amphibians and aquatic vascular plants is exceeded only at a 60% drift scenario with RQs of 1.68 and 1.2 respectively. This occurs when MCPB is applied aerially for pasture weed control at a rate of 1.700 kg a.i./ha. Table 9-2 summarizes the refined drift risk assessment of MCPB for aquatic organisms.

5.0 Value

5.1 Commercial Class Products

5.1.1 Commercial Class Uses for Which Information on the Value of MCPB is Sought

Appendix III lists those uses of MCPB that the registrants continue to support but that have risk concerns as a result of re-evaluation.

Due to the proposed phase out of dry/field peas and aerial application, the PMRA is requesting feedback on:

- Extent of aerial application of MCPB in cereals and pastures;
- Potential impact of the proposed phase out of the use on dry/field peas and of aerial application of MCPB in cereals and pastures;

- Availability, viability and extent of use of alternative active ingredients registered for use on dry/field peas and aerial application on cereals and pastures;
- Availability, effectiveness and extent of use of non-chemical weed management practices in cereals and pastures and on dry/field peas.

5.2 Domestic Class Products

There are no Domestic Class products containing MCPB registered in Canada.

5.3 Value of MCPB

MCPB continues to contribute to weed management in a variety of crops when used in accordance with the label directions. It is one of the few post-emergent herbicides that control a broad spectrum of annual and perennial broadleaf weeds in peas (dry/field and succulent/processing). MCPB is co-formulated with MCPA to broaden the spectrum of weed control. When formulated with MCPA, it is the only alternative to 2,4-DB registered for use in seedling clovers (wild white, Dutch white, ladino, alsike, and red clovers) alone or with a companion crop (wheat, barley and oats). It is one of the few post-emergent herbicides for use in seedling grasses and in seedling alfalfa grown for seed production. MCPB also plays a role in mitigating resistance development in weeds to other herbicide groups when used in rotation with them.

6.0 Toxic Substances Management 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. CEPA-toxic or equivalent, predominantly anthropogenic, persistent and bio-accumulative).

During the review process, MCPB and its transformation products were 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:

- MCPB does not meet Track 1 criteria, and is not considered a Track 1 substance. See Table 10, Appendix IX for comparison with Track 1 criteria.
- MCPB is not expected to form any transformation products that meet all Track 1 criteria.
- The use of MCPB is not expected to result in the entry of TSMP Track-1 substances into the environment.

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

6.2.1 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 MCPB and the end-use product Tropotox Selective Weedkiller liquid herbicide as well as other formulations of MCPB do not contain any formulants of health or environmental concern identified in the *Canada Gazette.*

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].

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for MCPB is adequate to define the majority of toxic effects that may result from exposure to MCPB. MCPB is not expected to be genotoxic or carcinogenic under conditions of typical use. The most sensitive effects following oral exposure to non-pregnant animals is kidney and liver toxicity.
A low incidence of cranio-facial malformations of the fetus has been observed following exposure of the pregnant animal to MCPB. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests when the proposed mitigation measures are considered.

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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.

7.1.1 Occupational Risk

The mixer/loader and applicator risks were not of concern for most crops provided that risk mitigation measures were applied. The mixer/loader and applicator risks were of concern for dry/field peas even when feasible risk mitigation measures were considered. All aerial scenarios are risks of concern. Assuming a single application per year, post-application risks were not of concern for all scenarios provided that risk mitigation measures were applied.

For seedling grasses, the calculated MOE did not reach the target of 300 based on an area treated per day of 100 hectares. However, a restriction on the amount handled of 111 kg a.i./day, which corresponds to approximately 85 hectares for this crop, would be considered acceptable to address the risk concern.

7.1.2 Dietary Risk from Food and Drinking Water

The calculated acute and chronic dietary (food + drinking water) risks are not of concern.

7.1.3 Non-Occupational Risk

MCPB is not registered for use in any residential areas; therefore, a non-occupational risk assessment was not required.

7.1.4 Aggregate Risk

The calculated aggregate risk from food and drinking water are not of concern.

7.2 Environmental Risk

MCPB has a short half-life in soil and aquatic systems under aerobic conditions and it is not persistent in the environment. Although it is water soluble and is predicted to leach into groundwater, soil column tests and monitoring studies indicated that this was not substantiated to the same extent. No bioconcentration is likely to occur in non-target organisms. MCPB can pose an acute dietary risk to some bird guilds feeding on freshly treated leafy foliage and other food items. Similarly, certain small wild mammals may be adversely affected on an acute basis by consumption of treated food items and thus, mitigative toxicity label statements are recommended. Amphibians may be at risk in shallow seasonal water bodies based on extrapolated toxicity data. MCPB poses a risk to terrestrial plants from spray drift deposition off the site of application and to broadleaf dicotiledon plants such as woody shrubs, trees, etc. in particular. This is especially the case for pasture applications by aircraft, where up to 60% of the applied amount can drift off target and move considerable distances thereby affecting sensitive plants. The required mitigation measure to reduce risk to non-target plants from MCPB exposure is the use of calculated buffer zones as described in Appendix X.

7.3 Value

MCPB continues to contribute to weed management in a variety of crops when used in accordance with the label directions. It is one of the few post-emergent herbicides that control a broad spectrum of annual and perennial broadleaf weeds in peas (dry and succulent). MCPB is co-formulated with MCPA to broaden the spectrum of weed control. When formulated with MCPA, it is the only alternative to 2,4-DB registered for use in seedling clovers (wild white, Dutch white, ladino, alsike and red clovers) alone or with a companion crop (wheat, barley and oats). It is one of the few post-emergent herbicides registered for use in seedling grasses and in seedling alfalfa grown for seed production. MCPB also plays a role in mitigating resistance development in weeds to other herbicide groups when used in rotation with them.

The PMRA is specifically requesting information on the feasibility of restricting the maximum amount of MCPB that can be handled per day to 111 kg a.i./day for all uses of MCPB. For all crops except seedling grasses, this limit would be 70 ha/day at a maximum rate of 1.594 kg a.i./day or area treated proportionally adjusted according to the labelled crop and application rate. For seedling grasses, this limit would be 85 ha/day at the maximum application rate of 1.313 kg a.i./ha.

Due to the proposed phase out of dry/field peas and aerial application, the PMRA is requesting feedback on:

- Extent of aerial application of MCPB in cereals and pastures;
- Potential impact of the proposed phase out of the use on dry/field peas and of aerial application of MCPB in cereals and pastures;
- Availability, viability and extent of use of alternative active ingredients registered for use on dry/field peas and aerial application on cereals and pastures;
- Availability, effectiveness and extent of use of non-chemical weed management practices in cereals and pastures and on dry/field peas.

8.0 Proposed Regulatory Decision

After a thorough re-evaluation of the herbicide MCPB, Health Canada's PMRA, under the authority of the *Pest Control Products Act,* is proposing continued registration for the sale and use of MCPB and associated end-use products for certain uses supported by the technical registrant, provided that the mitigation measures for health and environment described in this document are implemented and the required confirmatory data are provided within a specified timeframe.

The uses of MCPB products proposed for continuing registration, together with proposed mitigation measures and use limitations, are presented in Appendix X.

8.1 Proposed Regulatory Actions

8.1.1 Proposed Regulatory Action Related to Human Health

For agricultural uses, the PMRA has determined that worker risks during mixing, loading and application and during post-application activities are acceptable for all uses, except dry/field peas, provided that the mitigation measures listed in this section are implemented. Thus, dry/field peas and all aerial applications are being proposed for phase out as they pose a risk of concern despite feasible mitigation measures. For seedling grasses, a restriction on the amount handled of 111 kg a.i./day is proposed which equates to approximately 85 hectares at the maximum application rate for this crop.

Due to lack of residue data in grass and cereal feedstuffs, as well as a confined crop rotation trial study, restrictive label statements are being proposed with regard to grazing and cutting those crops for hay as well as crop rotation.

8.1.1.1 Toxicological Information

The label text of technical, manufacturing concentrate and commercial class products containing MCPB must include the following text:

Toxicological Information
High concentrations of MCPB may cause severe irritation to the eyes. Symptoms of overexposure to MCPB could include slurred speech, twitching, jerking and spasms, drooling, low-blood pressure and unconsciousness. Treat symptomatically.

8.1.1.2 Proposed Mitigation for Dietary Exposure

Restrictions on grazing treated crops and cutting for hay are proposed, pending submission of residue data on grass and cereal feedstuffs (forage, hay, straw, etc.). See Appendix X for details.

Restrictions on crop rotation are proposed, pending submission of an acceptable confined crop rotation trial study. See Appendix X for details. Until the study is submitted, rotation should be limited to crops on which MCPA or MCPB use is registered. The need for a field crop rotation trial study will be determined following the review of the confined trial study.

8.1.1.3 Proposed Mitigation for Mixer, Loader and Applicator Exposure and Post-Application Exposure

Based on exposure assessments described in Table 1 of Appendix VI, recommendations to mitigate exposure include the proposal to add personal protective equipment, engineering controls, restricted entry intervals, and limiting the amount of active ingredient handled per day (See below and Appendix X for details). By limiting the amount handled per day, aerial application in cereals and pastures are not feasible; thus, application of MCPB by air is proposed for phase out.

As part of the proposed engineering controls, all solutions must be packaged in a closed mix/load system. A closed mix/load system is defined as a procedure for removing a pesticide from its original container, rinsing the emptied container and transferring the pesticide and rinse solution through connecting hoses, pipes and coupling that are sufficiently tight to prevent exposure of any person to the pesticide or rinse solution.

The "closed system" must have the following attributes:

- Be made of materials appropriate for use with pesticides and a pressurized system;
- Have gauges protected against breakage;
- Have shut-off valves to prevent chemical from spilling when the hose is disconnected.

Feasible mitigation measures were not determined for mixers/loaders and applicators for dry/field peas and any aerial application scenarios, hence phase out of these uses is proposed. For seedling grasses, a restriction on the amount handled per worker of 111 kg a.i./day is proposed which equates to approximately 85 hectares at the maximum application rate for this crop.

8.1.1.4 Residue Definition for Risk Assessment and Enforcement

At present, there is no residue definition (RD) for MCPB under the PCPA. The proposed RD for MCPB is the sum of the free and conjugated forms of MCPB and MCPA for plant and animal commodities. The USEPA considers the same compounds in its RD for MCPB. Codex has no RD or MRLs specified for MCPB.

8.1.1.5 Maximum Residue Limits for MCPB in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian maximum residue limits and to remove MRLs that are no longer supported. The PMRA recognizes, however, that interested parties may want to retain an MRL in the absence of a Canadian registration to allow legal importation of treated commodities into Canada. The PMRA requires similar chemistry and toxicology data for such import MRLs as those required to support Canadian food use registrations. In addition, the PMRA requires residue data that are representative of use conditions in exporting countries, in the same manner that representative residue data are required to support domestic use of the pesticide. These requirements are necessary so that the PMRA may determine whether the requested MRLs are needed and to ensure they would not result in unacceptable health risks.

Where no specific MRL is established for a pest control product under the *Pest Control Product Act* (PCPA), subsection B.15.002(1) of the Food and Drug Regulations applies. This requires that residues do not exceed 0.1 ppm, which is considered as a General MRL for enforcement purposes. However, changes to this General MRL may be implemented in the future, as indicated in Discussion Document DIS2006-1, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the General MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set for the concerned commodities.

MRLs for all food uses of MCPB are currently regulated by B.15.002(1) of the Food and Drug Regulations which specifies that residues are not to exceed 0.1 ppm. Specific MRLs are proposed for peas (dry/field and succulent/processing), wheat grain, barley grain and corn grain at 0.1 ppm while the remaining registered commodities will continue to be regulated by the 0.1 ppm default.

8.1.2 Proposed Regulatory Action Related to Environment

The risk assessment identified a risk of adverse effects to non-target terrestrial plants, birds, mammals and aquatic organisms. In order to mitigate this risk, buffer zones were determined for terrestrial and aquatic systems. The determined buffer zones ranged from 1 – 3 m for ground application, and 3 – 175 m for aerial application (See Appendix X).

8.1.3 Proposed Regulatory Action Related to Value

No regulatory action is proposed from the standpoint of value.

The application rate of 1.751 kg a.i/ha, which is used exclusively on peas, is no longer supported by the registrant and thus will be discontinued

An amendment to the label, based on the PMRA's database as of February 19, 2009 arising from the re-evaluation of this active ingredient, is proposed in Appendix X.

8.2 Additional Data Requirements

8.2.1 Data Requirements Related to Chemistry

The following confirmatory data is required for continued registration of MCPB:

DACO 2.13.4	Impurities of human health or environmental concern This active ingredient is suspected to contain e.g. polychlorinated dibenzodioxins and furans. Analytical data on these contaminants were provided but are outdated.

Recent analytical data from at least five batches of the TGAI must be provided 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.

List of Abbreviations

µg	micrograms
ADI	acceptable daily intake
a.i.	active ingredient
ARfD	acute reference dose
atm	atmospheres
bw	body weight
CFIA	Canadian Food Inspection Agency
cm	centimetre(s)
d	day(s)
DACO	data code
DEEM®	Dietary Exposure Evaluation Model
DER	Data Evaluation Report
DFR	dislodgeable foliar residue
DT_{50}	dissipation time to 50% (the dose required to observe a 50% decline in the test population)
DWLOC	drinking water level of comparison
DNA	deoxyribonucleic acid
EChE	erythrocyte cholinesterase
EEC	expected environmental concentration
EP	end-use product
EXAMS	Exposure Analysis Modeling System
F_0	parental animals
F_1	first filial generation
F_2	second filial generation
g	gram(s)
GAP	good agricultural practice
GC-FPD	Gas Chromatography-Flame Photometric Detector
GC-MSD	Gas Chromatography-Mass Selective detector
GC-NPD	Gas Chromatography-Nitrogen Phosphorous Detector
ha	hectare(s)
HAP	hours after application
Hg	mercury
IPM	integrated pest management
IRED	Interim Reregistration Eligibility Decision (USEPA Document)
K_d	adsorption coefficient
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50% (a concentration causing 50% mortality in the test population
LD_{50}	lethal dose to 50% (a dose causing 50% mortality in the test population)
LEACHM	Leaching Estimation and Chemistry Model
LOAEL	lowest observed adverse effect level
LOD	limit of detection

LOEC	lowest observed effect concentration
m	metre(s)
m^3	metre(s) cubed
mg	milligram(s)
min	minute(s)
mm	millimetre(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
OC	organic carbon
OP	organophosphate
PChE	plasma cholinesterase
PCPA	*Pest Control Product Act*
PDP	Pesticide Data Program (United States data)
PHI	preharvest interval
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
pKa	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppb	parts per billion
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
PRZM	Pesticide Root Zone Model
PSI	pre-slaughter interval
Q_1*	cancer potency factor
RED	Reregistration Eligibility Decision
REI	restricted entry interval
ROC	residue of concern
RQ	risk quotient
TC	transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
URMULE	User Requested Minor Use Label Expansion
USEPA	United States Environmental Protection Agency
USDA	United States Department of Agriculture
USFDA	United States Food and Drug Administration

Appendix I MCPB products registered in Canada (excluding discontinued products or products with a submission for discontinuation), as of February 19, 2009 based on the PMRA's Oracle database.

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee	
					MBS/MBT[1]	MAS[2]
5937	Commercial	Nufarm Agriculture Inc.	Tropotox Selective Weedkiller Liquid Herbicide	Solution	412 g/L	Not applicable
8211	Commercial	Nufarm Agriculture Inc.	Nufarm Tropotox Plus 400 Liquid Herbicide	Solution	375 g/L	25 g/L
22003	Commercial	United Agri Products Canada Inc.	Topside Contains MCPB and MCPA	Solution	375 g/L	25 g/L
24336	Commercial	Interprovincial Cooperative Limited	IPCO Clovitox Plus Liquid Herbicide	Solution	375 g/L	25 g/L
26488	Commercial	Interprovincial Cooperative Limited	Weedaway Clovitox Plus Liquid Herbicide	Solution	375 g/L	25 g/L
20754	Manufacturing concentrate	Nufarm Agriculture Inc.	MCPB Sodium Salt Herbicide	Solution	412 g/L	Not applicable
21808	Technical	A.H. Marks And Company Limited*	Marks MCPB Technical Acid	Solid	95.5%	Not applicable
27542	Technical	Nufarm Agriculture Inc.	Nufarm MCPB Technical Acid	Solid	97%	Not applicable

[1] MBS = MCPB (Present as sodium salt); MBT = MCPB
[2] MAS = MCPA (Present as potassium or as sodium salt)
* Owned by Nufarm UK Ltd. as of February 4, 2010.

Appendix II Commercial Class uses of MCPB registered in Canada as of February 19, 2009. Uses from discontinued products or products with a submission for discontinuation or products which the registrant wishes to discontinue are not included.[1]

Use Site Category	Sites		Weeds[2]	Maximum Application Rate (kg a.i./ha)	Application Equipment	Supported Uses?[3]
13 - Terrestrial feed crops	Pastures	Across Canada	Annual and perennial broadleaf weeds	1.594	Ground and/or aerial application equipment	Yes
	Seedling grasses[4]			1.313	Ground equipment only	
	Seedling alfalfa grown for seed production	Western Canada		1.594		Yes, Minor Use
7 - Industrial oil seed crops and fibre crops 13 - Terrestrial feed crops 14 - Terrestrial food crops	Field corn	Across Canada		1.594	Ground equipment only	Yes
13 - Terrestrial feed crops 14 - Terrestrial food crops	Cereals (wheat, oats, barley and rye)	Across Canada		1.594	Ground and/or aerial application equipment	Yes
	Peas (dry/field and succulent/processing)			1.751 [1.594]	Ground equipment only	
	Seedling clover (wild white, Dutch white, ladino, alsike, and red clovers) alone or with a companion crop (wheat, oats, and barley)			1.594		

1 All supported end-use products are formulated as solutions. Application is made once per year. Information on application equipment and the number of applications is based on both labels and that provided by the MCPB task force and or registrants. For peas (dry/field and succulent/processing), the rate of application in [ ] is the rate of application supported by the MCPB task force and later confirmed by the registrant that this rate will be reflected in the label amendment.

2 Weeds include: Wild mustard, ball mustard, wormseed mustard, stinkweed, ragweed, redroot pigweed, lamb's quarters, Canada thistle, bull thistle, curled dock, plantain, hempnettle, shepherd's-purse, annual sowthistle, flixweed, perennial sowthistle, field bindweed, horsetail, volunteer rapeseed (including canola), wild radish, creeping buttercup, tall buttercup.

3 Yes = use is currently registered and supported by the registrant.
Minor use = use was added as a User Requested Minor Use Label Expansion (URMULE).

4 Seedling grasses include: Seedling smooth bromegrass, meadow bromegrass, creeping red fescue, reed canary grass, altai fescue, meadow fescue, tall fescue, altai, wild ryegrass, Russian wild ryegrass, timothy, crested wheatgrass, intermediate wheatgrass, pubescent wheatgrass, tall wheatgrass, slender wheatgrass, streambank wheatgrass, northern wheatgrass, western wheatgrass and green needlegrass.

Appendix III Registered Commercial Class uses of MCPB in Canada for which risk concerns have been identified and information on value is sought

Use Site Category	Sites	Weeds[1]	Support[2]	Concerns from Risk Assessment[3]	Identification of Risk Assessment Concerns
13 - Terrestrial feed crops	Pastures	Annual and perennial broadleaf weeds	Yes	Partial (due to aerial application)	Aerial Application Proposed restrictions to amount of MCPB handled per day (i.e. 111 kg a.i./day) renders the use of aerial equipment unfeasible. This restriction affects application to pastures and cereals. Dry/field peas A risk of concern for workers was identified for mixing, loading or application of MCPB even with consideration of additional mitigation measures.
	Seedling grasses[4]		Yes	No	
	Seedling alfalfa grown for seed production		Yes, Minor use	No	
7 - Industrial oil seed crops and fibre crops 13 - Terrestrial feed crops 14 - Terrestrial food crops	Field corn		Yes	No	
13 - Terrestrial feed crops 14 - Terrestrial food crops	Cereals (wheat, oats, barley and rye)		Yes	Partial (due to aerial application)	
	Peas (dry/field)		Yes	Yes	
	Peas (succulent/processing)		Yes	No	
	Seedling clover (wild white, Dutch white, ladino, alsike, and red clovers) alone or with a companion crop (wheat, oats, and barley)		Yes	No	

[1] Weeds include: Wild mustard, ball mustard, wormseed mustard, stinkweed, ragweed, redroot pigweed, lamb's quarters, Canada thistle, bull thistle, curled dock, plantain, hempnettle, shepherd's-purse, annual sowthistle, flixweed, perennial sowthistle, field bindweed, horsetail, volunteer rapeseed (including canola), wild radish, creeping buttercup, tall buttercup.

[2] Yes = use is supported by the registrant; No = use is not supported by the registrant; Partial = the registrant partially supports the use pattern; and Minor use = use was registered as a User Requested Minor Use Label Expansion (URMULE).

[3] Yes = there are risk concerns for this use; No = there are no risk concerns for this use; and Partial = partial risk concern for the use (e.g. PMRA has risk concerns only for some application methods of the use).

[4] Seedling grasses include: Seedling smooth bromegrass, meadow bromegrass, creeping red fescue, reed canary grass, altai fescue, meadow fescue, tall fescue, altai, wild ryegrass, Russian wild ryegrass, timothy, crested wheatgrass, intermediate wheatgrass, pubescent wheatgrass, tall wheatgrass, slender wheatgrass, streambank wheatgrass, northern wheatgrass, western wheatgrass and green needlegrass.

Appendix IV Toxicology Endpoints for MCPB Health Risk Assessment

Table 1 Toxicology Endpoints, Uncertainty Factors and Composite Assessment Factors/Target Margin of Exposure

	RfD (mg/kg bw/day)	Study NOAEL (or LOAEL)	CAF or Target MOE and Rationale[1]
ARfD **females 13-49**	0.017	NOAEL: 5 mg/kg bw Rabbit Developmental Toxicity (cranio-facial malformations)	300 PCPA = 3-fold
ARfD **general population**	0.5	LOAEL: 146 mg/kg bw Rat Acute Neurotoxicity (ataxia)	300 PCPA = 1-fold UF_L = 3-fold
ADI **All populations**	0.017	NOAEL: 5 mg/kg bw/day Rabbit Developmental Toxicity (craniofacial malformations)	300 PCPA = 3-fold
short-term dermal **intermediate-term dermal**[2]		NOAEL: 5 mg/kg bw/day Rabbit Developmental Toxicity (cranio-facial malformations)	300 Occupational: Concern for unborn child = 3-fold
short-term inhalation **intermediate-term inhalation**[3]			

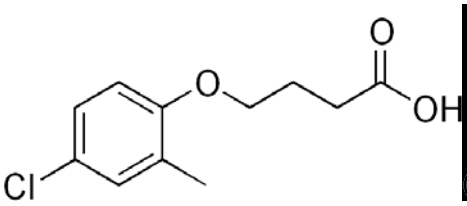
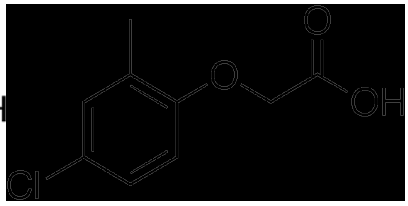
[1] CAF (Composite assessment factor) refers to the total of uncertainty and PCPA factors for dietary and residential risk assessments, MOE refers to target MOE for occupational assessments

[2] Since an oral NOAEL was selected, a dermal absorption factor of 51% or 75% is used in a route-to-route extrapolation.

[3] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) is used in route-to-route extrapolation.

Appendix V Toxicology Profile for MCPB.

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Study/Species	Results/Effects
Metabolism/Toxicokinetic Studies	
 **MCPB**  **MCPA**	
Rat (Oral)	**Absorption:** MCPB was well absorbed (~90%) in both dose groups (extensive elimination in urine). **Distribution:** An insignificant proportion of the administered dose was recovered from tissues (3.5%) and primarily recovered from carcass. Quantitative recovery for low (5 mg/kg bw/day) and high (100 mg/kg bw/day) dose was 96.01 ± 0.97% and 99.57 ± 1.17%, respectively. Radioactivity was not detected in whole blood, bone, skeletal muscle, heart, or thyroid in both doses and additionally no radioactivity was detected in the spleen, lungs, stomach, gonads, or adrenals at the low dose. Highest concentrations of radioactivity for low and high doses were found in fat (0.258 and 30.55 g/g, respectively) and skin (0.071 and 11.25 g/g), respectively). For 100 mg/kg bw/day dose group, clearance was less rapid. In high dose group animals, adrenals had high concentration of radioactivity (8.923 g/g) which may be due to presence of surrounding adipose that was not removed prior to analysis. A 20-fold increase in administered dose lead to ~120 fold increase in concentration in fat indicating preferential distribution to this tissue and/or slow clearance. Skin radioactivity was lower than in the fat, but there was ~160 fold increase at the high dose compared to the low dose. Based on the low percentage of the administered dose recovered from the tissues and carcass, it was believed that bioaccumulation potential is low. Furthermore, MCPA metabolism studies found that "Tissue levels of MCPA declined rapidly soon after the termination of dosing". 5 mg/kg: Carcass = 0.75 ± 0.34% administered dose, 0.043 ± 0.017 g/g. Concentration detected in other tissues - liver (0.139 g/g), kidney (0.055 g/g), residual carcass (0.043 g/g), plasma (0.023 g/g). Total radioactivity from tissue and carcass = 0.856 ± 0.318% of total recovered. 100 mg/kg: Carcass = 3.39 ± 1.59% of administered dose, 3.31 ± 1.47 g/g. Concentration in other tissues - liver (1.63 g/g), spleen (1.27 g/g), lung (0.86 g/g), kidney (0.74 g/g), gonads (0.70 g/g), stomach (0.41 g/g), and plasma (0.35 g/g). Radioactivity from tissue and carcass=3.52 ± 1.58% of total recovered radioactivity. **Metabolism:** 30 metabolites were identified by LC-MS, with 14 obtaining assigned structures (LC-MS used primarily for identification purposes). Using putative metabolite reference standards, MCPA and HMCPA were identified. Unidentified metabolites represented <2% of the administered dose. Metabolism appeared to be via 3 oxidative pathways: 1) Substitution on the parent molecule (minor pathway, principally involving conjugation with glycine), 2) Cleavage of the butyl moiety resulting in a phenol (occurs

Study/Species	Results/Effects
	following hydroxylation, free phenol not detected in urine, but assumed to be intermediate as sulphate and glucuronide conjugates were present), 3) Metabolism via β-oxidation (major pathway) leading to the loss of 2 carbons, forming acetic acid (MCPA). Note that formation of these metabolites through P-450 oxidation cannot be ruled out; however, the most important route of metabolism was through β-oxidation forming MCPA which then undergoes methyl hydroxylation to form HMCPA. This is consistent with known metabolism of MCPA, which is a major metabolite of MCPB. MCPA found in urine was 34.53% (low dose) and 38.57% (high dose) of the administered dose (TLC method). Using HPLC analysis, MCPA in urine was 35.70% and 32.98% in low and high doses, respectively. MCPA in feces was 0.5% and 2.21% in the low and high dose, respectively. HMCPA detected in urine was 5.31% (low dose) and 9.01% (high dose) of administered dose. No metabolites were observed to be unique to feces. At the low dose, 0.50% MCPA and 0.53% MCPB was observed. At the high dose, 2.21% MCPA and no MCPB was observed. **Excretion:** Urine was a major route of excretion with >84% eliminated within 48 hrs. Urinary elimination in 100 mg/kg dose group was slower. Feces were not a significant route of elimination compared to urine (5.45% and 10.66% excreted through feces for low and high dose groups, respectively). Radioactivity in expired air was below the limit of detection. 5mg/kg dose group - Urine: 0-12h= 67.85 ± 3.07%, 12-24h= 9.65 ± 2.19%, 24-48h= 2.56 ± 0.88% administered dose excreted (98% of total recovered activity). 81.45 ± 3.6% of administered dose recovered in urine, 89% including cage wash. Feces: 0-24h= 4.69 ± 0.83, 24-48h= 0.457 ± 0.15. Mean cumulative recovery = 5.45 ± 0.84% of administered dose. 86% was collected between 0-24h, after 72h < 0.03% collected. 100mg/kg dose group - Urine: 0-12h= 34.33 ± 5.43%, 12-24h= 24.86 ± 7.33%, 24-48h= 12.71 ± 5.48% of administered dose excreted, showing prolonged elimination compared to low dose group. Possibly due to saturable process during absorption or elimination. Excess is likely stored in fat based on tissue distribution data. Mean cumulative recovery of 76.53 ± 2.23% of administered dose, 84.33% including cage wash. Feces: 0-24h= 7.89 ± 1.37% of administered dose excreted, 24-48h= 2.20 ± 1.28%. Mean cumulative recovery = 10.66 ± 2.68%. 20 fold increase in dose lead to only 2 fold increase in feces excretion.

Study/Species	Results/Effects
Rat (Oral) - MCPA Studies	Rate and extent of absorption and excretion: T_{cmax} 2-4 h (5 mg/kg) to 6 h of dosing (100 mg/kg); 62-80% of the administered dose was excreted via urine by 24 hours (all dose regimens), 2-5% eliminated by fecal excretion. Slower renal clearance in the dog than in rats, mice, and humans. Pregnant mice (i.v.): lower concentrations in fetal tissues than maternal tissues, highest concentration in maternal kidney and visceral yolk sac. Distribution / target organ(s): Highest levels in ovaries and uterus (acid form only), skin, fat, kidney (0.1 g/g tissue at 96h post-dosing in 5 mg/kg group; 1-3 g/g tissue 192 h post-dosing in 100 mg/kg group); no evidence of bioaccumulation. Toxicologically significant compound(s): Acid form= 53-69% of low dose / 71-85% of high dose as MCPA, 12.5% HMCPA; Salt/ester forms: 72-78% MCPA, 12.5% HMCPA, no salt or ester forms in urine or feces. After initial hydrolysis to MCPA, metabolism appears identical in all 3 forms.
Acute Toxicity Studies	
Acute Oral Toxicity - Rats	LD50 = 680 mg/kg **Moderate Toxicity** Clinical symptoms include: hunched posture, lethargy, ataxia, ↓ respiration rate, laboured respiration, ↑ lacrimation, pilo-erection, ptosis, loss of righting reflex, hypothermia, dehydration, ↑ salivation.
Acute Oral Toxicity - Rats	LD50 = 1570 mg/kg **Slight Toxicity**
Acute Oral Toxicity - Rats	LD50 = 4300 mg/kg **Low Toxicity**
Acute Dermal Toxicity - Rats (2 Studies)	LD50 >2000 mg/kg bw **Low Toxicity**
Acute Inhalation Toxicity - Rats	LC50 > 1.14 mg/L **Slight Toxicity** Symptoms include: One death due to lung congestion, closing/partial closing of eyes, abnormal respiration, excessive salivation (consistent with moderately irritating aerosol), abnormal breathing, brown staining around snout and jaws, yellow/brown staining around urogenital area, lethargy.
Eye Irritation - Rabbits (3 studies)	**Minimal to Moderately Irritating**
Dermal Irritation - Rabbits (2 studies)	**Non-irritating**
Dermal Sensitization - Guinea Pigs (2 studies)	**Non-sensitizing**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Short-term Toxicity Studies			
MCPA 21-day dermal Rabbit - NZW 5/sex/dose	0, 10, 100, 1000 mg/kg bw/day Purity: ~94%	Dermal: 10 Systemic: 100	**≥100 mg/kg bw:** erythema, desquamation, diffuse acanthosis **1000 mg/kg bw:** hyperkeratosis, ↓body weight gain, renal tubule mineralization
90-Day Oral / Rat (Sprague-Dawley) 10/sex/dose	0, 6.3/7.1, 31.5/35.1, 158.4/178.2 mg/kg bw/d (100, 500, 2500ppm) Purity: 91.1%	6.3	**≥6.3/7.1 mg/kg bw:** ↑ alkaline phosphatase (♀) (non-adverse) **31.5/35.1 mg/kg bw:** ↓ body weight gain (♀), ↓ food consumption (♀), ↑ kidney weight (relative to brain) **158.4/178.2 mg/kg bw:** ↓ body weight,↓ body weight gain, ↓ food consumption, ↓ food efficiency, ↓ platelet count (♀s), ↓ alanine aminotransferase (♂), ↑ kidney weight (relative to brain weight.), ↑ creatinine (♂s, within historical range), ↑ alkaline phosphatatse (♂s), liver necrosis and chronic inflammation (♀s), kidney tubule degeneration and dilation, chronic kidney inflammation.
90-Day Oral / Dog Beagle 5/sex/dose	0, 0.36/0.42, 2.5/2.5, 25.1/26.1, 44.1/56.3 mg/kg bw/day) for ♂/♀ Purity: 91.1%	2.5	**≥2.5/2.5:** ↑ creatinine (♀) (non-adverse) **≥25.1/26.1:** ↓ glucose, ↑ urea nitrogen, ↑ creatinine, small prostate **44.1/56.3:** ↓ body weight, ↓ body weight gain, ↓ food consumption, ↓ food efficiency, ↓ red blood cells, ↓ hematocrit, ↑hemoglobin, ↓ platelets, ↓ lymphocyte, ↓ eosinophils, ↑ bilirubin, ↓ alkaline phosphatase, ↑ creatinine, ↓ urinary specific gravity (♂), ↑ liver to brain weight (♀), ↓ testes weight relative to brain weight, small testes, ↓ thymus weight relative to brain weight, lymphoid depletion, inactive prostate
MCPA 90-day dietary Dog, Beagle 4/sex/dose	0, 3, 12, 48 mg/kg bw/day Purity: 95-99 %	LOEL = 3.0	**≥3.0 mg/kg bw:** ↑ in phenol red retention, blood urea nitrogen and creatinine levels **≥12 mg/kg bw:** ↓body weight gain, distended gall bladder, mononuclear inflammatory cells in liver **48 mg/kg bw:** all dead/moribund- cachexia - multisystemic effects (animals showed conjunctivitis and corneal opacity)
	0, 0.3, 1.0, 12 mg/kg bw/day Purity: 94.6 % MCPA-P: 12 mg/kg bw/day Purity: 99.3 %	1.0 (0.8)	**12 mg/kg bw:**↑ blood urea nitrogen, creatinine, phenol red retention, ↓alkaline phosphatase, bile duct proliferation, kidney pyelitis, ↓ prostate/testes weight - similar changes with 12 mg/kg bw MCPA-P including: ↑ liver weight, SGPT & protein

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
MCPA 1-yr dietary Dog - Beagle 6/sex/dose	0, 6, 30,150 ppm (0, 0.22, 1.09, 5.51 mg/kg bw/day) Purity: 100%	NOEL = 0.22	**≥1.09 mg/kg bw:** ↑ blood urea nitrogen, creatinine, pigment deposits in kidney **5.51 mg/kg bw:** ↓body weight gain, ↑ thyroid weight, thyroid hyperplasia, stimulation
Neurotoxicity Studies			
MCPA Acid Acute Neurotoxicity Rat - Wistar 10/sex/dose	0, 150, 300, 600 mg/kg bw	150	**≥300 mg/kg bw:** ↓ body weight gain, ataxia, ↑ abdominal tension; **600 mg/kg bw:** ↓ open field activity, number of rearings, righting activity, motor activity - reversible, not selectively neurotoxic
MCPA DMAS Acute Neurotoxicity Rat - Wistar 10/sex/dose	0, 175 (146), 350 (292), 700 (583) mg/kg bw (acid equivalent)	LO(A)EL = 146	**≥146 mg/kg bw:** ataxia **≥292 mg/kg bw:**↑ abdominal tension **583 mg/kg bw:**↓ body weight gain, ↓ open field activity, motor activity - reversible, no neuropathy
MCPA 2-EHE Acute Neurotoxicity Rat - Wistar 10/sex/dose	0, 250 (167), 500 (333), 1000 (667) mg/kg bw (acid equivalent)	LO(A)EL = 167	**≥167 mg/kg bw:** ataxia, ↓ open field activity, righting activity, ↑ abdominal tension **≥333 mg/kg bw:** ↓ body weight gain, motor activity **667 mg/kg bw:** abdominal position ↓ in motor activity - reversible, no neuropathy
MCPA Acid 90-day dietary neurotoxicity Rat - Wistar 15/sex/dose	0, 50, 500, 2500 ppm (0, 3, 34, 177 mg/kg bw/day) Purity: 94.2%	3	No neuropathological findings. **≥34 mg/kg bw/day:** ↑ lipid storage in adrenal cortex. (♀): ↑ water intake, ↓ body weight gain (♂): ↓ triglycerides, ↑ relative kidney weight **177 mg/kg bw/day:** ↓ food consumption, body weight/body weight gain, motor activity, hemoglobin, hematocrit, platelets, calcium, glucose, total protein, globulins, triglycerides, absolute kidney weight; ↑ paleness, water consumption, mean corpuscular volume, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, foam cell accumulation in the lungs, myloid atrophy, hypocellular marrow, relative kidney weight, severe hypatocyte alterations with eosinophilic and granular cytoplasm. (♀): ↑ prothrombin time, thymic atrophy; ↓ albumin, urinary specific gravity. (♂): ↓ absolute and relative testes weight, rearings; ↑ water intake, urea, creatinine, testicular atrophy, bile duct hyperplasia, anisokaryosis, liver mitosis, aspermia/oligozoospermia of epididymis, atrophy of seminal vesicle and prostrate.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
MCPA-DMAS 90-day dietary neurotoxicity Rat - Wistar 15/sex/dose	0, 4 (3), 42 (34), 208 (168) mg/kg bw/day (acid equivalent) 917.5 g/L	3	No neuropathological findings. **≥34 mg/kg bw/day:** (♀): ↑ creatinine; (♂): ↑ kidney weight. **168 mg/kg bw/day:** ↓ Body weight/Body weight gain, food consumption, platelets, calcium, triglycerides; ↑ alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, necrosis in periportal hepatocytes, foam cell accumulation in lungs, hypocellular marrow. (♀): ↓ grip strength, red blood cells, hemoglobin, hematocrit, white blood cells, lymphocytes, glucose, urinary specific gravity; ↑ urine volume, liver weight, cytoplasmic eosinophilia, bile duct hyperplasia, myloid atrophy. (♂): ↑ γGT, cholesterol, magnesium, relative kidney weight, testicular atrophy (2/10), oligospermia in epididymis (1/10). Absolute brain weight ↓
MCPA 2-EHE 90-day dietary neurotoxicity Rat - Wistar 15/sex/dose	0, 5 (3.3), 54 (36), 261 (174) mg/kg bw/day (acid equivalent) Purity: 94.2%	3.3	No neuropathological findings. **≥36 mg/kg bw/day:** (♀): ↑ creatinine, water consumption. (♂): ↑ focal testicular; ↓ body weight/body weight gain, motor activity. **174 mg/kg bw/day:** ↓ food consumption, body weight/body weight gain, motor activity, red blood cells, mean corpuscular hemoglobin concentration, platelets, calcium, glucose, total bilirubin, triglycerides, absolute and relative brain weight; ↑ paleness, cataracts, opacity, lenticular degeneration, relative liver weight, mean corpuscular volume, mean corpuscular hemoglobin, alanine aminotransferase, alkaline phosphatase, creatinine, foam cell accumulation in the lungs, myloid atrophy, hypocellular marrow. (♀): ↑ striate thickening of the lens star, Aspartate aminotransferase, urinary vol, and relative kidney weight (♂): ↑ water intake, prothrombin times, testicular atrophy, aspermia/oligozoospermia in epididymides; ↓ WBC, lymphocytes, inorganic phosphate, total protein, globulins. Absolute brain weight ↓, relative brain weight ↑.
Chronic Toxicity/Oncogenicity Studies			
MCPA 2-yr dietary Mouse - B6F1:Crl BR 60/sex/dose	0, 20, 100, 500 ppm (0, 3.2, 15.7, 79.5 mg/kg bw/day) Purity 94.8-95.9%	NOEL = 3.2 NOAEL = 15.7	**≥15.7 mg/kg bw/day:** marginal ↓ body weight, heart weight (non-adverse at this dose) **79.5 mg/kg bw/day:** ↑ kidney weight, ↓ testes weight, kidney tubule casts, calcification, and nucleation of lymphocytes No evidence of oncogenicity

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
MCPA 2-yr dietary (1 yr interim) Rat - Wistar 75/sex/dose (10/sex/dose for interim sacrifice)	0, 20, 80, 320 ppm (0, 1.1, 4.4, 17.5 mg/kg bw/day) Purity 94.8-95.9%	17.5 No oncogenic effects up to 17.5 mg/kg bw	**4.4 mg/kg bw/day:**↓triglyceride levels (♂) at termination only, considered non-adverse. **17.5 mg/kg bw/day:** ↓triglycerides, ↑ alanine aminotransferase, ↓ liver weight. Moderate nephropathy (satellite group only, not seeing anything in the clinical chemistry or urinalysis, not seen worse than controls in the main group), iron storage in spleen noted at 12 months, not seen at termination Maximum tolerated dose not reached.
Reproductive and Developmental Toxicity Studies			
MCPA Multi-generation (Dietary) Rat - Crl:CD(SD)BR 25/sex/dose (2 litters/ generation)	0, 2.5, 7.5, 22.5 mg/kg bw/day Purity: 94.8%	Parental >22.5 Reproductive: NOAEL 22.5 *Offspring: >22.5	**≥ 2.5 mg/kg/day:** ↑ kidney weights, all doses (F_0 males), but no pathological findings (non-adverse) **22.5 mg/kg bw/day:** ↓ pup weight gain* (days 14-21 for F_1 and F_2, ↓ pup weight in F_2, on post-natal days 14 and 21. Maximum tolerated dose not reached. Reproductive: ↑ ovarian weights in F_0 and F_1 (♀) (non-adverse) *↓ pup weight was addressed with the submission of 2 one-generation reproduction screening studies on MCPA Acid and MCPA-2-EHE (see below). Both studies tested higher doses and showed a decrease in pup body weight on post-natal day 21 only. There was no effect on post-natal day 14, thus, the changes on pup body weight were considered to be a result of pup exposure via both lactation and treated solid diet. Based on all 3 studies, the PMRA NOAEL > 22.5 mg/kg bw/day.
MCPA-Acid (Range finding study) One-gen. (Dietary) Rat - Wistar 12/sex/dose	0, 36, 57, 75 (average acid equivalent during gestation; 0, 63, 99 or 122 at during lactation)		**≥36 mg/kg/day:** F_0♂- slight ↓ body weight; F_0♀ - ↑ kidney weight; F_1 - ↓ body weight (post-natal day 29-43), ↓ liver weight. **Reproductive**: ↓ ovary weight Based on body weight effects, maximum tolerated dose reached for F_1 adults. F_1 body weight effects did not occur until post-natal day 29, indicating **no sensitivity to young.** **Supplementary**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
MCPA 2-EHE (Range finding study) One-gen. (Dietary) Rat - Wistar 12/sex/dose	0, 54, 90, 126 (during gestation; 0, 92, 163, or 217 at during lactation)		**≥54 mg/kg/day:** F_0♂- slight ↓body weight; F_0♀ - ↑ kidney weight; F_1 - ↓ body weight (post-natal day 29-43), ↓ liver weight. **Reproductive**: ↓ gonad weight Based on body weight effects, maximum tolerated dose reached for F_1 adults. F_1 body weight effects did not occur until post-natal day 29, indicating **no sensitivity to young.** **Supplementary**
Developmental / Rat - Sprague Dawley Gavage 25/dose	0, 25, 100, 225 mg/kg/day (treated gestational day 6-15) Purity: 97.6% Vehicle: corn oil	Maternal: 25 Developmental: 25	Maternal: **≥ 25 mg/kg/day:** ↓ food consumption (gestational day 6-15) **≥100 mg/kg/day:** ↓ body weight (gestational day 15), ↓Body weight gain (gestational day 6-15), (gestational day 0-21), ↓corrected body weight gain (gestational day 0-21), ↓ food consumption (gestational day 6-15) **225 mg/kg/day:**↓Body weight 10% (gestational day 15 and day 21), ↓ corrected body weight (gestational day 0-21), ↓ body weight gain (gestational day 6-15), (gestational day 0-21), ↓ corrected body weight gain (gestational day 0-21), ↓food consumption (gestational day 6-15), alopecia (abdomen, chest, hips, hind legs, fore paws), ↓ gravid uterine weight. Developmental: **100 mg/kg/day:** ↓ fetal body weight (♂), reduced ossification **225 mg/kg/day:** ↓ fetal body weight, reduced ossification, cranio-facial malformations 1/147 (microstomia, cleft palate, lowset ears, agnathia, dome-shaped head), skeletal malformations 1/307 (fused cervical arches, exoccipital fused to cervical arch #1, tympanic annuli displaced, zygomatic arch misshapen, mandible missing, squamosal misshapen, ethmoid misshapen)
MCPA-Acid Teratogenicity Gavage Rat - Wistar 25/dose	0, 15, 60, 120 mg/kg bw/day Purity: 94.22%	Maternal: 60 Developmental: 60	Maternal: **120 mg/kg bw:** ↓body weight/body weight gain (corrected), food consumption, ↓ placental weight. Developmental: **120 mg/kg bw:** ↓ fetal weight, ↑ skeletal delays (including incomplete ossification of the skull, non-ossified sternebrae). No teratogenic effects.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
MCPA DMAS Teratogenicity Dietary Rat - Sprague-Dawley 25/dose	0,15, 50 and 150 mg/kg bw acid equivalent 754 g/L active ingredient (78.2% MCPA-DMA)	Maternal: 50 Developmental: 50	**Maternal:** **≥150 mg/kg bw:** one animal died *in extremis*, yellow and brown matting/staining in the urogenital area, red material around nose, ↓ defecation and hunched posture. After dosing (0-1 h), animals wiping mouths on cage floor, rocking, lurching or swaying;↓ body weight gain and food consumption; ↑ absolute and relative kidney weights, post-implantation loss and ↓ in viable litter size. **Developmental:** **≥50 mg/kg bw:** ↓ cervical centrum ossification **≥150 mg/kg bw:** ↑ skeletal malformations (bent limb bones, rib anomalies) and several skeletal variants (rudimentary ribs, delayed ossification).
MCPA 2-EHE Teratogenicity Dietary Rat - Sprague-Dawley 25/dose	0, 15, 40, 120 mg/kg bw acid equivalent Purity: 99.9%	Maternal: 40 Developmental: 40	**Maternal:** **≥120 mg/kg bw:** ↓ defecation, body weight/body weight gain (corrected), gravid uterine weight and food consumption; ↑ scabbing/hair loss in dorsal abdominal area, ↑ relative kidney weight (relative to body weight), ↑ in absolute kidney weight **Developmental:** **≥ 40 mg/kg bw:** ↑ delayed ossification **≥ 120 mg/kg bw:** ↓ mean fetal body weight, viable litter size, bent ribs (6.9% of litters for high-dose groups compared to 0.0 - 4.6% of the litters in historical controls); ↑ post-implantation loss/early resorption, hydrocephaly, bent limbs
Developmental / Rabbit - NZW Gavage 20/dose	0, 1, 5, 20 mg/kg/day (gestational day 6-18) Purity: 97.6% Vehicle: corn oil	**PMRA** Maternal: 5 Developmental: 5 **USEPA** Maternal: 5 Developmental: 20	Maternal: **20 mg/kg/day:** ↑mortality, body weight loss 2.6x↓ (gestational day 6-18), hypoactivity, paresis, paralysis, ataxia, loose feces, ↑incidence of colour change of liver and kidneys, abortions (post-treatment) Developmental: **20 mg/kg/day:** lowset ears, dilated lateral ventricle.
MCPA Teratogenicity Rabbit - Himalayan Gavage 15/dose	0, 15, 30, 60 mg/kg bw/day Purity: 94.22%	Maternal 30 Developmental: ≥60	Maternal: **60 mg/kg bw**: ↓body weight/body weight gain, ↓ food consumption Developmental: No fetal effects No teratogenic effects.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	Results/Effects
Genotoxicity Studies		
Mouse Bone Marrow Micronucleus Test - CD-1 10, 5, 5, 5, 10 ♂/dose (Positive control, control, 125, 250, 500 mg/kg, respectively)	0, 125, 250, 500 mg/kg dose volume:10mL/kg Purity: 96% Vehicle: phosphate buffered saline	Negative
Ames Salmonella Assay 3 plates/dose	5, 16.7, 50, 167, 500, 1670 µg/plate ± S9 Purity: 97.6% Solvent: EtOH	Negative
CHO/HPRT Mammalian cell forward gene mutation assay.	50, 100, 250, 500, 1000, 1500, 2000 µg/mL ± S9. Purity: 97.6% Solvent: EtOH	Negative
Mammalian cytogenetics - Chromosomal aberrations in CHO Cells	100, 600, 1000 µg/mL(-S9) 75, 350, 750 µg/mL(+S9) Purity: 97.6% Solvent: DMSO	Significant ↑ in numbers of aberrations/cell observed at 750 µg/mL with S9. Evidence of chromosomal aberrations at cytotoxic concentration with S9.
Other Genotoxic effects: Unscheduled DNA Synthesis in Rat Hepatocyte Primary Cell Culture	Prelim assay: 0.01, 0.03, 0.1, 0.3, 1, 3, 10, 30, 100, 300, 100, 3000 µg/mL Full assay: 0.01, 0.03, 0.1, 0.3, 1 µg/mL (cytotox found at doses ≥ 3 µg/mL, thus doses< 3 µg/mL were selected for scoring) Solvent: EtOH Purity: 97.6%	No evidence of unscheduled DNA synthesis

Appendix VI Agricultural Mixer/Loader/Applicator and Post-Application Risk Assessment

Table 1 MCPB Short-Intermediate Term Mixers/Loaders and Applicators Exposure and Risk Assessment

Crop	Scenario	Application Equipment	Form	PPE[e]	Max Rate (g a.i./ha)	Area Treated Per Day (ha/day)	Daily Exposure mg/kg/day		Margins of Exposure[c] (Target 300)		Combined MOE[d] (Target = 300)	Max kg ai handled per day to reach target MOE
							Dermal[a]	Inhalation[b]	Dermal	Inhalation		
USC 7, 13 & 14												
Field corn	Farmer: M/L/A	Groundboom - open mixing & open cab	SN	Baseline	1590	80	0.114644	0.004652	44	1075	42	18.5
	Custom: M/L/A			Baseline	1590	140	0.200626	0.008141	25	614	24	18.5
	Farmer: M/L/A	Groundboom-closed mixing & closed cab	SN	Mid-level	1590	80	0.019121	0.000309	261	16186	257	**110.9**
	Custom: M/L/A			Mid-level	1590	140	0.033462	0.000541	149	9249	147	**110.9**
USC 13, 14												
Dry/field peas, Seedling clover, Cereals (wheat, barley, rye, oats)	Farmer: M/L/A	Groundboom - open mixing & open cab	SN	Baseline	1590	100	0.143304	0.005815	35	860	34	18.5
	Custom: M/L/A			Baseline	1590	300	0.429913	0.017445	12	287	11	18.5
	Farmer: M/L/A	Groundboom-closed mixing & closed cab	SN	Mid-level	1590	100	0.023901	0.000386	209	12949	206	**110.9**
	Custom: M/L/A			Mid-level	1590	300	0.071703	0.001158	70	4316	69	**110.9**
Succulent/processing peas	Farmer: M/L/A	Groundboom - open mixing & open cab	SN	Baseline	1590	30	0.042991	0.001744	116	2866	112	18.5
	Farmer: M/L/A	Groundboom-closed mixing	SN	Baseline	1590	30	0.015332	0.000116	326	43162	324	n/a

Crop	Scenario	Application Equipment	Form	PPE[e]	Max Rate (g a.i./ha)	Area Treated Per Day (ha/day)	Daily Exposure mg/kg/day		Margins of Exposure[c] (Target 300)		Combined MOE[d] (Target = 300)	Max kg ai handled per day to reach target MOE
							Dermal[a]	Inhalation[b]	Dermal	Inhalation		
		& closed cab										
Cereals (wheat, barley, rye, oats)	M/L	Aerial- open mixing	SN	Baseline	1030	400	0.225747	0.009417	22	531	21	30.4
		Aerial- closed mixing		Maximum			0.034167	0.000647	146	7723	144	201
	Applicator	Aerial		Baseline			0.042642	0.000412	117	12136	116	**161**
USC 13												
Pastures	Farmer: M/L/A	Groundboom- open mixing, open cab	SN	Baseline	1590	100	0.143304	0.005815	35	860	34	18.5
	Custom: M/L/A			Baseline		300	0.429913	0.017445	12	287	11	18.5
	Farmer: M/L/A	Groundboom- closed mixing & closed cab	SN	Mid-level	1590	100	0.023901	0.000386	209	12949	206	**110.9**
	Custom: M/L/A			Mid-level		300	0.071703	0.001158	70	4316	69	**110.9**
	M/L	Aerial- open mixing	SN	Baseline	1030	400	0.225747	0.009417	22	531	21	30.4
		Aerial- closed mixing		Maximum			0.034167	0.000647	146	7723	144	201
	Applicator	Aerial		Baseline			0.042642	0.000412	117	12136	116	**161**

Crop	Scenario	Application Equipment	Form	PPE[e]	Max Rate (g a.i./ha)	Area Treated Per Day (ha/day)	Daily Exposure mg/kg/day		Margins of Exposure[c] (Target 300)		Combined MOE[d] (Target = 300)	Max kg ai handled per day to reach target MOE
							Dermal[a]	Inhalation[b]	Dermal	Inhalation		
USC 13												
Seedling grasses	Farmer: M/L/A	Groundboom-open mixing, open cab	SN	Baseline	1310	100	0.118068	0.004791	42	1044	41	18.5
	Custom: M/L/A			Baseline		300	0.354205	0.014373	14	348	14	18.5
	Farmer: M/L/A	Groundboom-closed mixing & closed cab	SN	Mid-level	1310	100	0.019692	0.000318	254	15716	250	**110.9**
	Custom: M/L/A			Mid-level		300	0.059076	0.000954	85	5239	83	**110.9**
USC 13												
Seedling alfalfa	Farmer: M/L/A	Groundboom-open mixing, open cab	SN	Baseline	1030	100	0.092832	0.003767	54	1327	52	18.5
	Custom: M/L/A			Baseline		300	0.278497	0.011301	18	442	17	18.5
	Farmer: M/L/A	Groundboom-closed mixing & closed cab	SN	Mid-level	1030	100	0.015483	0.000250	323	19989	318	**n/a**
	Custom: M/L/A			Mid-level		300	0.046449	0.000750	108	6663	106	**110.9**

Shaded cells indicate MOEs that are less than target.
Bolded numbers indicate values selected for amount of Kg handled per day to reach target MOE in risk assessment.
[a] Where dermal exposure µg/kg/day = (unit exposure x area treated x use rate (g a.i./ha) x 75 % dermal absorption)/70 kg bw
[b] Where inhalation exposure µg/kg/day = (unit exposure x area treated x use rate (g a.i./ha))/70 kg bw
[c] Dermal and inhalation MOE is based on a oral NOAEL of 5 mg/kg bw/day, target is 300.
[d] Calculated using the following equation: Combined MOE = NOAEL /(Exp Dermal + Exp Inhalation)
[e] Baseline = single layer (long sleeved shirt, long pants) and chemical resistant gloves for all M/L, no gloves for groundboom and aerial applicator. Mid-level PPE = coveralls over single layer and chemical resistant gloves, no gloves for groundboom applicator. Max PPE = chemical resistant coveralls over single layer, no gloves for aerial applicator.
SN = solution; M/L/A = mixer/loader/applicator; PPE = personal protective equipment

Table 2 Restricted Entry Intervals for Commercial Post-Application Activities – One Application

Crop	Activity	TC (cm^2/hr) [a]	Max Rate (g a.i./ha)	DFR ($\mu g/cm^2$) [b]	Max # of App.	Exposure Time (hr/day)	Dermal Exposure (Day 0) (mg/kg bw/day) [c]	Dermal MOE (Day 0) [d] Target = 300	Target DFR ($\mu g/cm^2$) [e]	REI (Days) [f]
Field Corn	Irrigation	1000	1590	3.18	1	8	0.1853	27	0.2859	23
	Scouting	400	1590	3.18	1	8	0.0741	67	0.7149	15
Pastures	Scouting	100	1590	3.18	1	8	0.0185	270	2.859	1
Seedling Grasses	Scouting	100	1310	2.62	1	8	0.0153	327	2.859	12 hours
Seedling Alfalfa	Scouting	100	1030	2.06	1	8	0.0120	416	2.859	12 hours
Seedling Clover	Scouting	100	1590	3.18	1	8	0.0185	270	2.859	1
Peas (dry/field and succulent/processing)	Scouting, rouging (hand weeding)	100	1590	3.18	1	8	0.0185	270	2.859	1
Cereals	Scouting	100	1590	3.18	1	8	0.0185	270	2.859	1

Shaded cells indicate MOEs that are less than the target MOE.

[a]Transfer coefficients are from the Science Advisory Council for Exposure Agricultural Transfer Coefficient document (Revised - August 7, 2000b)

[b]Dislodgeable Foliar Residue values were calculated using the standard default of 20% of the application rate for day 0 and 10% dissipation per day thereafter (values shown are for day 0 post-application).

[c]Dermal exposure on Day 0 was calculated using the following equation: TC (cm^2/hr) x Duration (8 hr/day) x DFR ($\mu g/cm^2$) x Dermal Absorption (51%)/ Body Weight (70 kg)

[d]Dermal MOE on Day 0 is the margin of exposure on the day of application. Based on short-intermediate term oral NOAEL of 5 mg/kg bw/day, target MOE is 300.

[e]Target DFR is the level below which dislodgeable foliar residue values need to be to reach target MOEs to perform post-application activities in treated areas. It is calculated using the following equation:

$$\underset{(\mu g/cm^2)}{DFR_T} = \frac{\text{NOAEL } (\mu g/kg) \times \text{BW (kg)}}{\text{TC } (cm^2/hr) \times \text{Exposure Time (hrs)} \times \text{Target MOE (unitless)} \times \text{Derm Abs (51\%)}}$$

[f]A restricted entry interval (REI) is the duration of time which must elapse before residues decline to a level where entry into a treated area to perform a specific activity will result in a margin of exposure above the agency target. The lowest REI permitted for occupational areas is 12 hours.

Appendix VII Dietary Exposure and Risk Estimates for MCPB

Table 1 Dietary Exposure and Risk Estimates of MCPB

Population Subgroup	Acute Dietary[1] (95th percentile)		Chronic Dietary[2]	
	Dietary Exposure (mg/kg bw)	%ARfD	Dietary Exposure (mg/kg bw/day)	%ADI
General Population (total)	N/A	N/A	0.000908	5
All Infants (< 1 year old)	0.025469	5	0.001754	10
Children 1-2 years old	0.011965	2.5	0.001686	10
Children 3-5 years old	0.010980	2	0.001708	10
Children 6-12 years old	0.007760	1.5	0.001222	7
Youth 13-19 years old	N/A	N/A	0.000876	5
Males 13-19 years old	0.006206	1	0.000968	6
Adults 20-49 years old	N/A	N/A	0.000800	5
Males 20-49 years old	0.006605	1	0.000797	5
Adults 50+ years old	0.005960	1	0.000691	4
Females 13-49 years old	0.006662	39	0.000758	4.5

[1]Acute Reference Dose (ARfD) of 0.5 mg/kg/day applies to all population subgroups except females 13-49 years old. Acute Reference Dose (ARfD) of 0.017 mg/kg/day applies to females 13-49 years old.
[2]Acceptable Daily Intake (ADI) of 0.017 mg/kg/day applies to the General Population & all subgroups.

Appendix VIII Food Residue Chemistry Summary

1.1 Metabolism

The nature of the residue in plant and animal commodities is adequately understood based on metabolism studies in peas, snap beans, and dairy cows. However, a metabolism study in a representative cereal crop may be needed to support additional uses or MRLs.

MCPB and MCPA are two chlorophenoxy herbicides which differ only in that MCPB contains two additional carbon atoms. Metabolic enzymes can remove those carbons during degradation, in a process called β-oxidation. This results in MCPB being converted to MCPA. In animal metabolism studies, both MCPB and MCPA were rapidly absorbed and excreted, with urine being the major route of excretion; no bioaccumulation occurred with either compound. For both compounds, the major urinary metabolite was MCPA. In plant metabolism studies, MCPB was shown to be converted to MCPA as well.

1.1.1 Plant metabolism

MCPB metabolism studies in peas have shown that MCPB is converted to MCPA by β-oxidation of the side chain. MCPB and MCPA undergo oxidation of the phenyl methyl and the resulting hydroxymethyl compounds form conjugates, including glucose conjugates. The major compound identified in mature pods and vines was the parent, MCPB, representing 40% and 72% of the total radioactive residue (TRR) in pods and vines, respectively. The compounds identified in mature seed included MCPA/MCPA ester (11% TRR) and the glucose conjugate of hydroxy MCPA (12.5% TRR). Polar unknowns comprised 27% of TRR.

According to the studies “Review on the Metabolism of Phenoxy Compounds in Plants and Animals” and “Metabolism of Pesticides”, after 3, 6 and 11-day interval, MCPB has been found to convert into MCPA in snap beans by the way of β-oxidation of the side chain. In cleavers (*Galium aparine*), by using ^{14}C and ^{36}Cl, most MCPA was found to convert into different compounds 10 days after application. These include CO_2 (7%), a water-soluble fraction retaining the side chain (10%) and a water-soluble metabolite containing the ring but not the side chain (75%). This indicates a breakage of the phenoxy link without significant evolution of CO_2. In general, phenoxybutyric acid herbicides are selective as they kill those plant species which can carry on this complete conversion chain from the parent, via MCPA to the other metabolites. Dicotyledonous plants (e.g. common beans, broad leaved weeds) have the appropriate enzymes to carry on this conversion. Monocotyledonous plants (e.g. cereals) are generally not affected. Hence MCPB is used to selectively control “dicot” weeds in “monocot” crops. Transgenic phenoxy herbicide-tolerant plants of any type may be protected. In particular, dicotyledonous crop plants, including beans, soybeans, cotton, peas, potatoes, sunflowers, tomatoes, tobacco, and fruit trees, that are currently known to be injured or killed by phenoxy herbicides, can be transformed so that they become tolerant to these herbicides. Monocotyledonous crop plants, such as corn, sorghum, small grains, sugarcane, asparagus, and grasses, which are less sensitive to phenoxy herbicides than dicotyledonous plants can also be transformed to increase their tolerance to these herbicides.

1.1.2 Animal metabolism

Since MCPB and its metabolite MCPA are used for broadleaf weed control in forage crops, it is essential to know the metabolism of these compounds when ingested by livestock as herbicide residues on forage.

Based on metabolism studies in cows fed MCPB and/or MCPA and lactating goats and hens fed MCPA, it is concluded that the qualitative nature of the residue in livestock is understood. MCPB was found to be extensively metabolized (>95%) and excreted through urine (~80%) and feces (6%) within 48 hours. The only significant metabolite found was MCPA (>30% of administered dose). Minor amounts of free and conjugated HMCPB (= hydroxymethyl derivative of MCPB) and HMCPA (= hydroxymethyl derivative of MCPA) were also present.

In another study, two Holstein cows were fed 2.5 and 5.0 ppm (based on a daily ration of 22.7 kg of feed) of MCPB mixed with the grain for one day. Another Holstein cow was fed 5.0 ppm MCPA. Total urine samples were collected the day before feeding (control sample) and daily for six days after feeding the herbicides. A gas liquid chromatographic (GLC) method with electron capture detection (ECD) was used to detect and quantify MCPB and MCPA. Because the electron capturing capability of both compounds is insufficient for detection, a modification by nitration and methylation of MCPB and MCPA was carried out before chromatography to increase sensitivity. The recoveries of 0.4 ppm MCPA spiked urine samples were in the range 75-119%. The method was sensitive to about 0.1 ppm of MCPA. Recovery in MCPB spiked urine samples was not satisfactory. It is assumed that contemporary methods with better sensitivities (see Appendix IV, Analytical Methods Section) would give better results. According to the reported results, the single dose of 5 ppm was nearly eliminated in the urine of the MCPA-fed cow within four days. The urinary MCPA concentration decreased to 0.95 ppm on the fourth day, with the maximum amount of 22.4 ppm occurring on day 3. However, in cows receiving 2.5 and 5.0 ppm of MCPB, no MCPB was detectable in the urine samples after the first day. Instead, amounts of MCPA were found in these samples at levels of 0.35 and 0.55 ppm, respectively, which represented 9.2 and 7.2% conversion (by enzyme-mediated β-oxidation) of MCPB to MCPA.

Following oral administration of uniformly ring-labelled [^{14}C] MCPA to lactating goats for 3 days at 832 and 694 ppm (~1.0x and 0.85x the maximum theoretical dietary burden), the total radioactive residues (TRR) were 0.160 ppm and 0.172 ppm in milk, 0.140 ppm and 0.159 ppm in fat, 0.099 ppm and 0.070 ppm in muscle, 0.886 ppm and 0.899 ppm in kidney, and 0.480 ppm and 0.455 ppm in liver, respectively. Extraction and characterization of residues were conducted on samples from the goat dosed at 694 ppm. MCPA was identified in milk (28.5% TRR, 0.046 ppm), fat (30.2% TRR, 0.042 ppm), muscle (22.3% TRR, 0.022 ppm), kidney (6.7% TRR, 0.060 ppm), and liver (4.9% TRR, 0.024 ppm). An MCPA-glycine conjugate was also identified in milk (53.9% TRR, 0.086 ppm). A major component in fat (30.3% TRR, 0.042 ppm), kidney (57.4% TRR, 0.509 ppm), and liver (50.5% TRR, 0.243 ppm) was tentatively identified as a nonchlorinated triglyceride conjugate of MCPA or a closely related analog. Attempts to identify a major component in muscle (48.4% of TRR, 0.048 ppm) were unsuccessful. The remaining unidentified components in milk and other tissues represented <6% of the TRR. It should be noted that MCPA doses administered in these studies were orders of magnitude higher than MCPA residue levels which may result from metabolic conversion of MCPB to MCPA in

animals and from the eventual co-formulation of MCPB with MCPA. Hence, residues of MCPA resulting from MCPB use are expected to be negligible.

Following oral administration of uniformly ring-labelled [^{14}C] MCPA to hens for 7 days at 100 ppm (~430x the maximum theoretical dietary burden), the TRR were equivalent to 0.032 ppm in egg whites, 0.220 ppm in egg yolks, 0.033 ppm in fat, 0.017 ppm in thigh muscle, 0.006 pm in breast muscle, and 0.085 ppm in liver. MCPA was the major component identified in egg white (90.3% TRR, 0.029 ppm), egg yolk (57.4% TRR, 0.127 ppm), fat (12.0% TRR, 0.004 ppm), thigh muscle (35.5% TRR, 0.006 ppm), and liver (78.2% TRR, 0.0663 ppm). A metabolite detected in egg yolk (10.5% TRR, 0.023 ppm), fat (1.3% TRR, 0.0005 ppm), breast muscle (8.4% TRR, 0.001 ppm), and liver (1.4% TRR, 0.0012 ppm) was found to consist of at least three components, one of which was tentatively identified as the di-MCPA ornithine conjugate. Remaining metabolites, which accounted for 1.6-8.2% TRR in eggs and tissues, were characterized as acid-labile conjugates. Based on these studies, it was concluded that there is a reasonable expectation that no residues of MCPA will occur with respect to poultry.

1.1.3 Residue Definition

At present, there is no residue definition (RD) for MCPB under the PCPA. The proposed RD for MCPB is the sum of the free and conjugated forms of MCPB and MCPA for plant and animal commodities.

1.1.4 Canadian and International MRLs

MRLs for all food uses of MCPB are currently regulated by B.15.002(1) of the Food and Drug Regulations which specifies that residues are not to exceed 0.1 ppm. Specific MRLs are proposed for peas, wheat grain, barley grain and corn grain at 0.1 ppm while the remaining registered commodities will continue to be regulated by the 0.1 ppm default.

In the US, MCPB is registered for use on peas and mint (peppermint and spearmint). A tolerance for negligible residues of MCPB has been established under 40 CFR §180.318(a) for peas at 0.1 ppm, expressed in terms of MCPB *per se*, pending amendment to include the metabolite MCPA. Tolerances for the combined residues, free and conjugated, of the herbicide MCPB and its metabolite MCPA have been established in/on peppermint and spearmint at 0.2 ppm. This amended residue definition is consistent with the PMRA's residue definition. There are no Codex MRLs.

Table 1 Canadian MRLs and International Tolerances/MRLs

Commodity	Proposed CND MRL (ppm)	US Tolerance (ppm)	Codex MRL (ppm)
Peas	0.1	0.1**	-
Wheat	0.1	-	-
Barley	0.1	-	-
Oats	*	-	-
Rye	*	-	-

Commodity	Proposed CND MRL (ppm)	US Tolerance (ppm)	Codex MRL (ppm)
Field corn	0.1	-	-
Alfalfa. seed	*	-	-
Peppermint	-	0.2***	-
Spearmint	-	0.2***	-

* Covered under Part B, Division 15, subsection B.15.002(1) of the FDR as 0.1 ppm.
**40 CFR §180.318(a)(1)); ROC = MCPB only
*** 40 CFR §180.318(a)(2)); ROC = MCPB + MCPA (both free and conjugated).

1.2 Analytical Methods

1.2.1 Supervised Residue Trial Analytical Methodology

Animals – A request for a waiver of the requirements for analytical methodology studies in animal matrices was submitted based on the low use of peas and pea products in animal feeding stuffs and the availability of methods analyzing for MCPA, a metabolite of MCPB. The PTRL East method of analysis (PTRL Project# 1000), as reflected in PMRA#s 1732987 and 1732988, using a gas chromatographic method with electron capture detection described for 2,4-DB (4-(2,4-dichlorophenoxy)butanoic acid), was modified to allow for quantification of MCPA in the presence of co-extractives using a mass-selective detector. The PTRL study shows that recoveries of MCPA fortified at approximately 0.01 and 0.1 ppm in milk ranged from 63 to 107%. The 63% recovery was observed in one of five samples fortified at the LOQ (0.01 ppm). Recoveries in the four remaining 0.01 ppm fortifications ranged from 70 to 87%. Recoveries for MCPA fortified at approximately 0.05 and 0.5 ppm in liver, kidney, muscle and fat ranged from 91 to 118%, 81 to 108%, 75 to 120% and 54 to 100%, respectively. The recovery of 54% was observed in one of five fat samples fortified at the LOQ (0.05 ppm). Recoveries in the four remaining 0.05 ppm fortified fat samples ranged from 75 to 87%. Since the method validation was accepted for the determination of the magnitude of residues of MCPA in milk and animal tissues, the waiver can be granted. For confirmatory purposes, the registrant is requested to submit to the PMRA an adapted version of the method (including validation data) allowing quantitation of MCPB.

Plants –An acceptable analytical method and validation data were submitted to the USEPA for MCPB, MCPA and 2-HMCPA in pea matrices. These data have been reviewed by the USEPA and are deemed adequate for enforcement purposes. The registrant is requested to submit the original data and/or the USEPA DERs to the PMRA for confirmatory purposes.

A previous PMRA review describes a gas liquid chromatography (GLC) – electron capture detection (ECD) method which was submitted for detection of MCPB and MCPA in green peas, vines and pods. The method involved nitration of MCPB and MCPA before chromatography to improve sensitivity. Briefly, MCPB and MCPA were extracted from macerated tissues with a solution containing acetone and 85% orthophosphoric acid. After basification with NaOH and subsequent evaporation to dryness, the dried material was redissolved in water and then acidified with HCl and 10% phosphotungstic acid and extracted with benzene. The benzene extract was washed through an aluminium oxide column and eluted with distilled ether and distilled chloroform. After drying, the column was eluted with a 1% $NaHCO_3$ solution. The bicarbonate

eluate was acidified, extracted with benzene and evaporated to dryness. For nitration, a freshly prepared 1% solution of $NaNO_3$ in 85% orthophosphoric acid was added to the dried benzene extract. After the mixture being heated on a steam bath, the nitration reaction was quenched by adding 2% Na_2SO_4. Distilled benzene was used again for extraction before evaporation to dryness. The residue was then esterified by addition of 10% BF_3-methanol and heating. After cooling, the mixture was partitioned with redistilled Skellysolve F. One microliter aliquots of Skellysolve layer were used for chromatography. It was mentioned that pyridine hydrochloride could be used instead of esterification and that the residue could be extracted from tissues with a mixture of benzene and glacial acetic acid. This mixture would then be washed with 1N NaOH to extract MCPB, MCPA and methylchlorophenol into the aqueous phase. After acidification, the sample would then be esterified and ready for chromatography. Quantitation was performed with an electron capture detector. Recoveries were in the range 70-97% at spike levels ranging from 0.2 to 20 ppm (MCPB alone or combined with MCPA, calculated as MCPB acid equivalents). The data suggests a limit of quantitation (LOQ) of 0.04 ppm.

A "Gas Chromatographic/Mass Spectrometric Method for Analysis of Chlorophenoxy Acid Herbicides: MCPB and MCPA in Peas" has been published in open literature. The method, based on other published methods, utilizes liquid-liquid partitioning, derivatization of the acids with diazomethane, Florisil® column cleanup, and gas chromatography/mass spectrometry detection. Method validation recoveries for 0.01, 0.1 and 0.5 ppm spike levels were found satisfactory for both MCPB and MCPA. Method sensitivity was established at 0.01 ppm.

The method titled "Analytical Method for the Determination of MCPA, HMCPA and MCPB in Cereals and Grass" submitted to the PMRA for the purpose of this re-evaluation was found incomplete. Method validation data are missing. The registrant is requested to submit this data. However, a previous PMRA review describes summarily an acceptable method for MCPB residue determination in wheat, barley and corn. The sample was macerated in water and then diluted by refluxing with NaOH to ensure extraction of free and bound material. The hydrolysate was neutralized and extracted with chloroform. Cleanup was performed by solvent partitioning, ion exchange chromatography and alumina column chromatography. Residues were then nitrated and determined by GLC-ECD. The sensitivity was <0.1 ppm. Recoveries were between 68 and 71% for barley spiked at 0.1 ppm, between 72 and 89% for wheat spiked at 0.1 ppm (84% at 0.5 ppm) and between 69 and 72% for corn spiked at 0.2 ppm.

Also, a GC-MSD (mass specific detection) method for the determination of MCPA 2-Ethylhexyl Ester (MCPA 2-EHE) and MCPA Dimethylamine Salt (MCPA DMAS) and their metabolites in wheat grain and flour was submitted to and reviewed by the USEPA. Samples were extracted with basic methanol and the extract was adjusted to pH 5 and then hydrolyzed with beta-glucosidase. The hydrolysate was partitioned with diethyl ether, and the diethyl ether fractions were concentrated, mixed with a sulfuric acid:methanol solution, and heated overnight at 37 °C, to convert MCPA and MCPA metabolites to their methyl esters. The methyl esters were partitioned into hexane and analyzed by GC-MSD. The reported LOQ was 0.02 ppm for each analyte in wheat grain and flour.

It is concluded that the requirements for analytical methods for the determination of residues of MCPB/MCPA in registered plant commodities are fulfilled. However the registrant is requested to submit the studies which are not in the PMRA database.

1.2.2 Enforcement Analytical Methodology

Animals – The PTRL East method of analysis (PTRL Project#1000) has been proposed by the registrant for both data collection and enforcement purposes. The method was previously reviewed for MCPA evaluation purposes and deemed adequate. The method is accepted for the purpose of the present evaluation but, for confirmation, the registrant is requested to submit to the PMRA an adapted version (including validation data) allowing quantitation of MCPB.

Plants – Data on a GC-MS analytical method have been reviewed by the USEPA and deemed adequate for enforcement purposes. The registrant is requested to submit the original data and/or the USEPA DER to the PMRA.

1.2.3 Independent Laboratory Validation (ILV)

The analytical methods referred to in Section 1.2.2 were reviewed by the USEPA and deemed acceptable. They can therefore be considered as having undergone adequate inter-laboratory validation.

1.2.4 Multi-Residue Analytical Method (MRM)

No MRM testing data were submitted by the registrant. However, the PESTRAK database dated 6/05 (PAM Volume I, Appendix I) indicates that recovery of MCPB is complete (70-106%) using multi-residue methods 402 E1 and 402 E2 or small (4-13%) using multi-residue method 402 (methods for acids and phenols). Recovery of MCPA is variable (60-131%) using method 402. The database did not include any information for any of the other test methods. The USEPA Residue Chemistry Chapter of the Registration Standard for MCPA, dated 8/31/81, noted that the PAM Vol. I method is adequate for enforcement of tolerances for residues of MCPA in livestock commodities as-is but recommended that the method be modified with a hydrolysis step (to release conjugated residues) for enforcement of MCPA tolerances in plant commodities. The same recommendation is applicable to MCPB MRL enforcement methods in plant commodities.

1.3 Food Residues

1.3.1 Storage Stability

1.3.1.1 Storage Stability of Working Solutions in Analytical Methodology

There is no test data on storage stability of MCPB and MCPA working solutions on file. In method validation studies, it is only stated that MCPB and MCPA standards were stored at -20 °C to 6 °C when not in use. Characterization and assignment of an expiry date were carried out before storage. The standards were used before the expiry date but no stability test was conducted before use. The registrant is requested to submit storage stability of working solutions for MCPB and its metabolite MCPA to the PMRA.

1.3.1.2 Freezer Storage Stability

A concurrent storage stability study was conducted with peas in three pea matrices (with pods, without pods and dried) fortified at 1 ppm for both MCPB and its metabolite MCPA. MCPB and MCPA appeared to be stable in frozen conditions (at unspecified temperature) over a period of 895 days for peas with and without pods and 852 days for dried peas. Recoveries in all matrices ranged from 77% to 91% for MCPB and from 68% to 78% for MCPA. A USEPA Data Evaluation Record (DER) on storage stability of MCPA in wheat grain and flour indicates that residues of MCPA are stable in/on wheat grain for up to 369-378 days and in wheat flour for up to 539 days in frozen conditions.

1.3.2 Crop Residues

1.3.2.1 Supervised Residue Trial Studies

Field trials for the determination of the magnitude of MCPB residues were conducted in US pea growing regions. The use pattern was one pre-flowering broadcast application at a nominal rate of 1.68 kg a.e./ha which is comparable to the Canadian registered rate of 1.59 kg a.e./ha. Three pea matrices (peas with pods, peas without pods and dried pea seeds) were analyzed for both MCPB and its metabolite MCPA using the analytical method referenced as Rhône Poulenc Report # 200283 “Analytical Method for the Determination of residues of MCPB and its metabolite MCPA in Peas”. Residues of MCPB were found to be below the limit of detection (LOD) of 0.01 ppm in all pea matrices at a minimum PHI of 30 days. Residues of MCPA were also below the LOD except in one dried pea sample at 0.0174 ppm. Based on the combined residues (MCBP and MCPA) detected (<0.02 ppm) in peas with and without pods and the combined residues detected (0.03 ppm) on dried peas, it is concluded that the data is sufficient to support a combined (MCPB + MCPA) maximum residue limit of 0.1 ppm. For peas with and without pods, concurrent recoveries from 0.1 ppm MCPB and MCPA fortified samples were in the range 87% -102% (MCPB samples) and 72%-84% (MCPA samples). For dried peas, concurrent recoveries from 0.01 ppm MCPB and MCPA fortified samples were in the range 84%-90% and 69%-75%, respectively.

Other field trial data for the determination of the magnitude of MCPB residue in peas were reviewed by the Canadian regulatory authority along with a GLC-ECD analytical method for data collection. The data (trial regions unspecified) were for the determination of residues in/on green peas of several varieties, with application rates of 1.12, 1.4, 2.24 and 2.8 kg a.e./ha and at PHIs varying from 0 to 46 days. It was noted that the data supports the registrant’s claim “no residue of either MCPB or MCPA was detected at PHI > 30 days in vines, unshelled peas (i.e. peas with pods) and pods alone”.

Field trial data for the determination of MCPB residues in cereals (wheat, barley and corn) were previously reviewed by the PMRA and found adequate. The use pattern was one application at 1.77 kg a.e./ha and PHIs of 55 days for wheat grain, 57 days for barley grain and 113 days for corn grain. It was noted that the data indicates no residues are likely to be detected in grain at the specified PHIs. The sensitivity of the analytical method was <0.1 ppm. Recoveries were between 68 and 71% for barley grain spiked at 0.1 ppm, between 72 and 89% for wheat grain spiked at 0.1 ppm (84% at 0.5 ppm) and between 69 and 72% for corn grain spiked at 0.2 ppm.

There are no field trial data for alfalfa seed and hay on file. The registrant is required to submit supervised residue trial studies for alfalfa to the PMRA.

1.3.2.2 Residue Decline Study

Concurrent residue decline studies included in field trial studies referred to in Section 1.3.2.1 indicate that residues of MCPB will be below the limit of detection (<0.01 ppm) in all pea matrices at a minimum PHI of 30 days. Residues of MCPA will also be below the LOD except in dried peas at 0.0174 ppm, still below the General MRL of 0.1 ppm. No residues are likely to be detected in wheat grain, barley grain and corn grain at 55, 57 and 113-day PHI, respectively. Residue decline studies for alfalfa seed are outstanding. The registrant is required to submit residue decline studies for alfalfa seed to the PMRA.

1.3.2.3 Confined Crop Rotation Trial Study

There are no confined crop rotation trial data on file. To minimize potential transfer of residues to secondary crops, a minimum rotational plant back interval (PBI) of 12 months must be observed for all crops other than those registered for use with MCPA or MCPB. The registrant can submit the outstanding study if shorter PBIs are necessary. Based on the current residue definition, the study should monitor both MCPB and MCPA.

1.3.2.4 Field Crop Rotation Trial Study

The need for a field crop rotation trial study will be determined following the review of the outstanding MCPB confined crop rotation trial study. Based on the current residue definition, the study should monitor both MCPB and MCPA.

1.3.2.5 Processed Food/Feed

There are no processing studies on file. DEEM-FCID™ default processing factors were used in the dietary exposure and risk assessments for MCPB.

1.3.2.6 Residue Data for Crops used as Livestock Feed

Data from residue trials on clover, conducted in 1989 and 1990 in Ontario, Manitoba, Saskatchewan and Alberta, were previously reviewed for the establishment of a 30-day PHI on immature crops for grazing or cutting for hay. Treatment consisted of a single application at a rate of 1.7 kg a.e./ha (1.594 kg MCPB a.e./ha + 0.106 kg MCPA a.e./ha) equivalent to the maximum application rate. Samples collected in 1989 were analyzed only for MCPB residues by a GC-MS method with an LOD of 0.1 ppm. The 1990 samples were analyzed for both MCPB and MCPA by a GC-MS method with an LOD of 0.05 ppm. Residues of MCPA were found to be below 0.1 ppm in all samples. MCPB residues ranged from 0.05 ppm to 0.5 ppm with an average of 0.16 ppm. Residue studies on all other potential feedstuffs are outstanding. Therefore, a restrictive label statement is proposed with regard to grazing and cutting those crops for hay until submission of acceptable data.

1.3.3 Livestock, Poultry, Egg and Milk Residue Data

In a published study, cows were fed a complete ration containing MCPA at six levels from 10 to 1000 ppm for 2 or 3 weeks at each level. Milk and cream samples were collected at predetermined intervals during the feeding of the chemical and for 7 days following withdrawal of the highest level. Residues of the acid and its phenol moiety were extracted with diethyl ether, separated by liquid chromatography on alumina, and determined as ester and phenol by electron capture or microcoulometry gas chromatography with an LOQ of 0.05 ppm and recoveries of >80%. The average residue found in milk at the highest feeding level were <0.05 ppm 2-methyl-4-chlorophenoxyacetic acid and 0.06 ppm 2-methyl-4-chlorophenol. The residues decreased rapidly upon removal of the chemical from the feed.

From another feeding study in which MCPA was fed to a cow at a level of 50 ppm for four days, it was found that milk samples, obtained daily during the four days of dose administration and for two days thereafter, had non-quantifiable amounts of MCPA (using a GC-ECD method with a sensitivity of 0.1 ppm). Based on this data and considering the comparatively low level of residues found in residue trials on cereals and clover (see Sections 1.3.2.1 and 1.3.2.6), it is concluded that the use of MCPB/MCPA on those crops (at the registered rate) will not result in residues above 0.1 ppm in milk.

A previous PMRA review reports on a livestock feeding study in which a 500 ppm MCPA containing ration fed to beef calves and sheep resulted in residues of only 2.3 ppm in kidneys of cattle, 0.12 ppm in liver of cattle and 0.82 ppm in the kidneys of sheep after 24 hours. After 7 days, the residue in kidneys of cattle decreased to 0.15 ppm. No residues of MCPA were detected in muscle and fat of cattle and in muscle, fat and liver of sheep after 24 hours. Based on this data and considering the comparatively low level of residues found in residue trials on cereals and clover (see Sections 1.3.2.1 and 1.3.2.6), it is concluded that the use of MCPB/MCPA on those crops (at the registered rate) will not result in residues above 0.1 ppm in livestock tissues and organs. In other words, if a total conversion of MCPB to MCPA in animals is assumed, there is a reasonable expectation that residues of MCPB/MCPA in all livestock and dairy commodities will not exceed the General MRL or the established US MCPA tolerance of 0.1 ppm.

From metabolism studies in hens [see Section 1.1.2], it is concluded that there is a reasonable expectation that no residues of MCPA will occur with respect to poultry. Based on this data and considering the comparatively low level of residues found in residue trials on cereals [see Section 1.3.2.1], it is concluded that the current use pattern of MCPB/MCPA will not result in quantifiable residues in poultry tissues, organs and eggs.

Appendix IX

Table 6-0 Transformation Products of MCPB in Environmental Fate Studies

Table 6-1 Fate and Behaviour of MCPB in the Terrestrial Environment

Property	Value	Transformation Products	Classification	Reference
Abiotic transformation				
Hydrolysis	-	-	Stable	
Phototransformation on soil	$t_{1/2}$ = 30 d	No major products	Not an important route of transformation in the environment	
Biotransformation				
Biotransformation in aerobic soil	DT_{50} = 8d	No major products	Non-persistent	
Biotransformation in anaerobic soil	$t_{1/2}$ = 8.3d	MCPA	Non-persistent	
Mobility				
Adsorption / desorption in soil	K_{oc} = 31-371	-	Moderate to very high mobility	
Soil leaching	<1% to 75% of applied	-	Low to high mobility, dependent on OM content	
Volatilization	-	-	Not volatile	
Field studies				
Field dissipation	-	-	Not available	

Table 6-2 Fate and Behaviour of MCPB in the Aquatic Environment

Study Type	Value	Transformation Products	Classification	Reference
Abiotic transformation				
Hydrolysis	-	-	stable	
Phototransformation in water	$t_{1/2}$ = 2.6 d	1) 4-(4-hydroxy-o-tolyloxy) butyric acid; 2) 2,4-dihydroxy phenyl formate; 3) O-cresol; 4) Benzoic acid; 5) 2-hydroxyphenyl formate.	Important route of transformation in the environment. Only products 1-3 exceed 10% in pH 7 water.	
Biotransformation				
Biotransformation in aerobic water systems	$t_{1/2}$ = 8.7-18 d	MCPA	Slightly persistent	
Partitioning				

Study Type	Value	Transformation Products	Classification	Reference
Adsorption / desorption in sediment	K_{oc} = 371	-	Moderately mobile	
Field studies				
Field dissipation	-	-	Not available	

Table 7-1 Effects on Terrestrial Organisms

Organism	Exposure	Endpoint Value	Degree of Toxicity[a]	Reference
Invertebrates				
Earthworm	Acute	7 day LD_{50} = 382 mg/kg soil NOEC = 95 mg/kg soil (mortality)	-	
Bee	Oral			
	Contact	LD_{50} > 25 ug/bee	Practically non-toxic	
	Brood / hive	N/A	-	
Other arthropod	Contact	EC_{50} = 2 kg as./ha[d]	-	
Parasitic arthropod	Contact	N/A	-	
Birds				
Bobwhite quail	Acute	LD_{50} = 257 mg/ kg bw	Moderately toxic	
	Dietary	LD_{50} = > 4500 mg/kg dw, NOAEL = 1250 mg/kg dw	Practically non toxic	
	Reproduction	N/A		
Mallard duck	Acute	N//A		
	Dietary	LD_{50} = > 4500 mg/kg dw, NOAEL = 1250 mg/kg dw	Practically non toxic	
	Reproduction	N/A		
Mammals				
Rat	Acute	LD_{50} = 912-> 2000 mg/kg bw/d	Slightly toxic	
	Dietary	N/A	-	
	Reproduction	N/A	-	
Mouse	Acute	N/A	-	
	Dietary	N/A	-	
	Reproduction	N/A	-	
Rabbit	Acute	N/A	-	
	Dietary	N/A	-	
	Developmental	NOAEL = 5 mg/kg dw LOAEL = 20 mg/kg dw, Maternal tox. only	-	

Organism	Exposure	Endpoint Value	Degree of Toxicity[a]	Reference
Vascular plants				
Vascular plant	Seedling emergence[b]	Monocot: onion EC_{25} = 22.4 g a.i./ha Dicot: cabbage EC_{25} = 18 g a.i./ha SSD HC_5 (based on EC_{50}) = 56 g a.i./ha	-	
	Vegetative vigour[c]	Monocot: onion EC_{25} = 18 g a.i./ha Dicot: tomato EC_{25} = 1.9 g a.i./ha SSD HC_5 (based on EC_{50}) = 22 g a.i./ha[e]	-	

[a] Atkins et al. (1981) for bees and USEPA classification for others, where applicable, [b] shoot length, [c] shoot weight [d] European Commission, (2005); [e] SSD HC_5 is the 5th percentile concentration derived from a Log-logistic equation (Model: ETX 2) based on EC_{50} data sets.

Table 7-2 Effects on Aquatic Organisms

Organism	Exposure	Endpoint Value	Degree of Toxicity[a]	Reference
Freshwater species				
Daphnia magna	Acute	LC_{50} = 50 mg a.e./L	Slightly toxic	
Rainbow trout	Acute	LC_{50} =3.9 mg a.i./L	Moderately toxic	
	Chronic	-		
Bluegill sunfish	Acute	LC_{50} =12.7 mg ai./L	Slightly toxic	
	Chronic	-		
Freshwater alga	Acute (cell density) 1. *Selenastrum* 2 *Anabaena* 3 *Navicula* Acute (Biomass) 1. *Selenastrum* 2 *Navicula*	EC_{50}/NOEC 0.38/<0.31 mg a.e../L >1.9/1.9 mg a.e./L 0.65/0.044 mg a.e./L E_bC_{50} 41 mg a.e/L 1.5 mg a.e./L	-	
Vascular plant	Dissolved *Lemna gibba*	EC_{50} = 0.21 mg a.e./L Frond production (USEPA) EC_{50} = 0.1.55 mg a.e/L Frond biomass (USEPA) E_bC_{50}=37 mg a.e./L Frond Biomass (EUROPEAN COMMISSION, (2005))	-	
	Over-spray	N/A	-	

Organism	Exposure	Endpoint Value	Degree of Toxicity[a]	Reference
Marine species				
Marine alga *Skeletonema costatum*	Acute (cell density)	1.36/0.10 mg a.e./L		

Table 8-1 Summary Of Endpoints Used In The Risk Assessment With Appropriate Conversions

Organism	Exposure	Endpoint	Value
Earthworm	Acute	14d-LC_{50}	191 mg a.i./kg soil
Bee	Contact	48h-LD_{50}	>25 ug/bee > 28 kg/ha
Beneficial Insects	-	EC_{50}	2000 g/ha
Birds (Bobwhite quail)	Acute	LD_{50}	25.7 mg/kg bw
	Chronic	5d-LD_{50} (LC_{50} converted to dose)	47.7 mg/kg bw
	Reproduction	Xd-NOEL (NOEC converted to dose)	N/A
Small bird (20g) (Default values based on Bobwhite quail)	Acute	LD_{50}	25.7 mg/kg bw
	Chronic	5d-LD_{50} (LC_{50} converted to dose)	47.7 mg/kg bw
Mallard duck	Chronic	5d-LD_{50} (LC_{50} converted to dose)	25.4 mg/kg bw
Mammals (Rat)	Acute	LD_{50}	91.2 mg/kg bw
	Chronic	Xd-LD_{50} (LC_{50} converted to dose)	NA
	Reproduction	NOEC	NA
Terrestrial vascular plants Based on SSD of plants	Seedling emergence	7d-EC_{50}	56 g a.i./ha
	Vegetative vigour	7d-EC_{50}	22 g a.i./ha
Freshwater invertebrates	Acute	96h-LC_{50}	25 mg/L
	Chronic	-	-
Freshwater fish Rainbow trout	Acute	96h-LC_{50}	0.39 mg/L
	Chronic	-	-
	ELS	Xd-NOEC	NA
Amphibians (based on R. trout data)	Acute	96h-LC_{50}	0.39 mg/L
	Chronic	-	-
Aquatic vascular plants (Lemna sp)		7d-EC_{50}	0.1 mg/L
Algae (Selenastrum)		7d-EC_{50}	0.19 mg/L
Saltwater algae		7d-LC_{50}	1.39 mg/L

Table 8-2 Screening Level Risk Assessment For MCPB Herbicide To Terrestrial Invertebrates And Vascular Plants (Including Tier I Drift Refinement For Plants)

Organism	Exposure	Endpoint Value	EEC	RQ	Risk LOC[4] Exceeded
Invertebrates					
Earthworm	Acute	14-day LC_{50} ÷ 2 191 mg ai./kg soil	0.76 mg a.i./kg soil	<0.01	No
Bee	Oral	N/A			
	Contact	28 kg a.i./ha (>25 ug a.i./bee)	1.70 kg a.i./ha	0.06	No
	Brood / hive				
Predatory arthropod	Contact	EC_{50}: 2 kg a.i./ha	1.70 kg a.i./ha	0.88	No
Parasitic arthropod	Contact	N/A	-	-	-
Vascular plants					
Screening Level Risk					
Vascular plant	Seedling emergence	EC25: 19 g a.i./ha	1.70 kg a.i./ha	**89.4**	Yes
	Vegetative vigour	EC25: 1.9 g a.i./ha	1.70 kg a.i./ha	**894**	Yes
	Tier I Refined Risk				
				Deposition Rate Off Field	
	Seedling emergence	SSD HD_5 56 g a.i./ha	1.70 kg a.i./ha	100 % / **30.3**	6% / **1.8**	23% / **6.96**	60%[5] / **18.1**	Yes
	Vegetative vigour	SSD HD_5 22 g a.i./ha	1.70 kg a.i./ha	**77.3**	**4.6**	**17.8**	**46.3**	Yes

[1]The LD50 in µg/bee is converted to the equivalent rate in kg/ha by multiplying 1.12 according to Atkins et al. (1981)
[2]Estimated Environmental Concentration (EEC)
[3]Risk Quotient (RQ) = exposure/toxicity
[4]Level of Concern (LOC) Shaded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment.
[5] 60% drift occurs for non-crop (pasture) applications only and at a rate of 1594 g a.i./ha.

Table 8-3 Screening Level Risk Assessment (On-Field) and Tier I Assessment (Off-Field) On Non-Target Birds and Mammals For MCPB Herbicide Assuming An Application Rate Of 1x 1.700 kg a.i./ha.

Exposure Type	Toxicity (mg a.i./kg bw)	Food Guild	On-Field		Off-Field*	
			EDE	RQ	EDE	RQ
Small Bird (0.02 kg)						
Acute	25.7	Insectivore (small insects)	85.6595	**3.3331**	5.1396	0.2000
		Granivore	21.4150	0.8333	1.2849	0.0500
		Fructivore	42.8300	**1.6665**	2.5698	0.1000
Dietary	47.7	Insectivore (small insects)	85.6595	**3.3724**	5.1396	0.2023
		Granivore	21.4150	0.8431	1.2849	0.0506
		Fructivore	42.8300	**1.6862**	2.5698	0.1012
Reproduction	N/A	Insectivore (small insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-
Medium Sized Bird (0.1 kg)						
Acute	25.7	Insectivore (small insects)	66.8480	**2.6011**	4.0109	0.1561
		Granivore	16.7121	0.6503	1.0027	0.0390
		Fructivore	33.4242	**1.3006**	2.0054	0.0780
Dietary	47.7	Insectivore (small insects)	66.8480	**1.4014**	4.0109	0.0841
		Granivore	16.7121	0.3504	1.0027	0.0210
		Fructivore	33.4242	0.7007	2.0054	0.0420
Reproduction	NA	Insectivore (small insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-

Exposure Type	Toxicity (mg a.i./kg bw)	Food Guild	On-Field		Off-Field*	
			EDE	RQ	EDE	RQ
Large Sized Bird (1 kg)						
Acute	25.7	Insectivore (large insects)	4.8793	0.1899	0.2928	0.0114
		Granivore	4.8793	0.1899	0.2928	0.0114
		Fructivore	9.7585	0.3797	0.5855	0.0228
		Herbivore (short grass)	69.7528	**2.7141**	4.1852	0.1628
		Herbivore (long grass)	42.5895	**1.6572**	2.5554	0.0994
		Herbivore (forage crops)	64.5363	**2.5111**	3.8722	0.1507
		Herbivore (leafy foliage)	131.4629	**5.1153**	7.8878	0.3069
Dietary	25.4	Insectivore (large insects)	4.8793	0.1921	0.2928	0.0115
		Granivore	4.8793	0.1921	0.2928	0.0115
		Fructivore	9.7585	0.3842	0.5855	0.0231
		Herbivore (short grass)	69.7528	**2.7462**	4.1852	0.1648
		Herbivore (long grass)	42.5895	**1.6768**	2.5554	0.1006
		Herbivore (forage crops)	64.5363	**2.5408**	3.8722	0.1524
		Herbivore (leafy foliage)	131.4629	**5.1757**	7.8878	0.3105
Reproduction	N/A	Insectivore (large insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-
		Herbivore (short grass)	-	-	-	-
		Herbivore (long grass)	-	-	-	-
		Herbivore (forage crops)	-	-	-	-
		Herbivore (leafy foliage)	-	-	-	-

Exposure Type	Toxicity (mg a.i./kg bw)	Food Guild	On-Field		Off-Field*	
			EDE	RQ	EDE	RQ
Small Mammal (0.015 kg)						
Acute	91.2	Insectivore (small insects)	49.2682	0.5402	2.9561	0.0324
		Granivore	12.3171	0.1351	0.7390	0.0081
		Fructivore	24.6342	0.2701	1.4781	0.0162
Dietary	N/A	Insectivore (small insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-
Reproduction	N/A	Insectivore (small insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-
Medium Sized Mammal (0.035 kg)						
Acute	91.2	Insectivore (small insects)	43.1896	0.4736	2.5914	0.0284
		Granivore	10.7975	0.1184	0.6478	0.0071
		Fructivore	21.5949	0.2368	1.2957	0.0142
		Herbivore (short grass)	154.3584	**1.6925**	9.2615	0.1016
		Herbivore (long grass)	94.2478	**1.0334**	5.6549	0.0620
		Herbivore (forage crops)	142.8146	**1.5659**	8.5689	0.0940
		Herbivore (leafy foliage)	290.9187	**3.1899**	17.4551	0.1914
Dietary	N/A	Insectivore (small insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-
		Herbivore (short grass)	-	-	-	-
		Herbivore (long grass)	-	-	-	-
		Herbivore (forage crops)	-	-	-	-
		Herbivore (leafy foliage)	-	-	-	-

Exposure Type	Toxicity (mg a.i./kg bw)	Food Guild	On-Field		Off-Field*	
			EDE	RQ	EDE	RQ
Reproduction	N/A	Insectivore (small insects)	-	-	-	-
		Granivore	-	-	-	-
		Fructivore	-	-	-	-
		Herbivore (short grass)	-	-	-	-
		Herbivore (long grass)	-	-	-	-
		Herbivore (forage crops)	-	-	-	-
		Herbivore (leafy foliage)	-	-	-	-
Large Sized Mammal (1 kg)						
Acute	91.2	Insectivore (large insects)	5.7694	0.0633	0.3462	0.0038
		Granivore	5.7694	0.0633	0.3462	0.0038
		Fructivore	11.5389	0.1265	0.6923	0.0076
		Herbivore (short grass)	82.4788	0.9044	4.9487	0.0543
		Herbivore (long grass)	50.3598	0.5522	3.0216	0.0331
		Herbivore (forage crops)	76.3106	0.8367	4.5786	0.0502
		Herbivore (leafy foliage)	155.4476	**1.7045**	9.3269	0.1023

*Assuming 6% drift for ground applications

Shaded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

[1] Endpoints were divided by an Uncertainty Factor to account for varying protection goals (i.e. protection at the community, population, or individual level)

[2] EEC: For birds and mammals, the EEC takes into account the maximum seasonal cumulative rate on vegetation and is calculated using PMRA standard methods based on the Hoerger and Kenaga nomogram as modified by Fletcher (1994)

EDE = Estimated dietary exposure; calculated for each bird or mammal size based on the EEC on appropriate food item for each food guild (at the screening level, the most conservative EEC for each food guild was used). The EDE was calculated using the following formula: (FIR/BW) x EEC. For each body weight (BW), the food ingestion rate (FIR) was based on equations from Nagy (1987). For generic birds with body weight less than or equal to 200 g, the "passerine" equation was used; for generic birds with body weight greater than 200 g, the "all birds" equation was used; for mammals, the "all mammals" equation was used:

Passerine Equation (body weight ≤200 g): FIR (g dry weight/day) = 0.398(BW in g) $^{0.850}$

All Birds Equation (body weight > 200 g): FIR (g dry weight/day) = 0.648(BW in g) $^{0.651}$

All Mammals Equation: FIR (g dry weight/day) = 0.235(BW in g) 0.822

[3] RQ = exposure/toxicity; RQs < 0.1 were not calculated to show all decimal points

[4] Conversion from a concentration (EEC) to a dose (EDE): [EDE (mg ai/kg bw) = EEC (mg ai/kg diet)/BW (g) x FIR (g dry weight/day)] Nagy, K.A. 1987. Field metabolic rate and food requirement scaling in mammals and birds. Ecological Monographs 57:111-128

Table 9-1 Screening Level Risk And Tier I Runoff Risk To Aquatic Organisms Exposed To MCPB Applied At 1.700 kg a.i./ha

Organism	Exposure	Endpoint value*	EEC	RQ	LOC Exceeded
Freshwater species					
Daphnia magna	Acute	25 mg/L	0.2 mg/L	0.008	No
	Chronic	-	0.2 mg/L	-	No
Rainbow trout	Acute	0.39 mg/L	0.2 mg/L	0.51	No
	Chronic	-	0.2 mg/L	-	No
Bluegill sunfish	Acute	1.27 mg/L	0.2 mg/L	0.11	No
	Chronic	N/A	0.2 mg/L	-	No
Freshwater alga	Acute	0.19 mg/L	0.2 mg/L	1.05	Yes
Vascular plant	Dissolved	0.1 mg/L	0.2 mg/L	2	Yes
	Over-spray	NA	-	-	
Amphibians	Acute	0.39 mg/L	1.1 mg/L	2.8	Yes
Marine species					
Marine alga	Acute	1.39 mg/L	0.2 mg/L	0.14	No
Tier I refined assessment for runoff into a 15 cm deep water body					
Amphibians	Acute	0.39 mg/L	0.36 mg/L	0.92	No

*Uncertainty factor applied
Shaded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.
[1]Estimated Environmental Concentration (EEC) on in water.
[2]Risk Quotient (RQ) = exposure/toxicity. For fish, RQ = EEC in an 80 cm deep water body / (EC50 ÷ 10 or LC50 ÷ 10); for a chronic exposure: RQ = EEC in an 80 cm deep water body / NOEC; for amphibians, the EEC in a 15 cm deep water body is used. For aquatic invertebrates and plants, RQ = EEC in a 80 cm deep water body / (EC50 ÷ 2 or LC50 ÷ 2); for a chronic exposure: RQ = EEC in a 80 cm deep water body / NOEC [3]Level of Concern (LOC).

Table 9-2 Tier I Refined Risk Assessment For Aquatic Organisms For Off-Field Spray Drift

Organism	Exposure	Endpoint Value[1]	Use Rate	Screening EEC	RQ		
					Drift Deposition Rate		
					6%	23%	60%
Freshwater Species							
Amphibians[2]	Acute	96-h LC_{50} ÷ 10 (0.39 mg a.i/L)	1.700 kg a.i./ha	1.1 mg a.i/L	0.17	0.64	**1.68**
Vascular plant	Dissolved	0.1 mg/L	1.700 kg a.i./ha	0.2 mg/L	0.12	0.46	**1.2**

[1] Endpoints were divided by an Uncertainty Factor to account for varying protection goals (i.e. protection at the community, population, or individual level).
[2] Endpoints from fish used as surrogate.
Shaded cells indicate that the RQ exceeds the LOC, triggering a refined risk assessment and further characterization where possible.

Table 10 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		MCPB Endpoints
CEPA toxic or CEPA toxic equivalent1	Yes		Yes
Predominantly anthropogenic2	Yes		Yes
Persistence3	Soil	Half-life ≥ 182 days	8 days (aerobic soil)
	Water	Half-life ≥ 182 days	8.7-18days (hydrolysis; aerobic water5)
	Sediment	Half-life ≥ 365 days	no
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life or volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on the vapour pressure [4 x 10-7 mm Hg (25ºC)] and Henry's Law Constant (2.734x10-11 atm. m3mol-1) 1/H= 3.65E10
Bioaccumulation4	Log KOW ≥ 5		1.3
	BCF ≥ 5000		N/A
	BAF ≥ 5000		N/A
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.

[1]All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e. all other TSMP criteria are met).
[2]The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.
[3] If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.
[4]Field data (e.g. BAFs) are preferred over laboratory data (e.g. BCFs) which, in turn, are preferred over chemical properties (e.g. log K_{OW}).
[5]It assumed that MCPB is stable in aerobic water based on the stability demonstrated in the anaerobic sediment and that an aerobic soil biotransformation study was not provided. A No information was provided on the fate of MCPB in aerobic water.

Appendix X Label Amendments for Products Containing MCPB

The following label amendments are required for technical, manufacturing and end-use products as applicable.

A) Number of Allowable Applications

A maximum of one application is allowed per season when applying products containing MCPB.

B) Label Changes Relating to Human Health

The label text of technical, manufacturing concentrate and commercial class products containing MCPB must include the following text:

> ***Toxicological Information***
> *High concentrations of MCPB may cause severe irritation to the eyes. Symptoms of overexposure to MCPB could include slurred speech, twitching, jerking and spasms, drooling, low-blood pressure and unconsciousness. Treat symptomatically.*

Uses requiring mitigation:

- Mitigation measures are required in order to reduce the risk of occupational exposure and labels should be amended to reflect the remaining registered MCPB uses: cereals (wheat, barley, oats, and rye), field corn, pastures, seedling grasses, seedling alfalfa, seedling clover, and succulent/processing peas.
- The following use is proposed for phase out and must be removed from the label:
  - Dry/field peas.

Application Rates:

- The application rate of 1.751 kg a.i./ha, which is used exclusively on peas, is no longer supported by the registrant and must be removed.

Use Precautions:

- The following warning statements should appear on the label of the technical product:

> *WARNING POISON: Harmful or fatal if swallowed*
> *CAUTION POISON: harmful if inhaled*
> *WARNING - eye irritant: Causes eye irritation, DO NOT get into eyes.*

- There may be potential for exposure to bystanders from drift following pesticide application to agricultural areas. In the interest of promoting best management practices and to minimize human exposure from spray drift or from spray residues resulting from drift, the following label statement is required:

  Apply only when the potential for drift to areas of human habitation or areas of human activity (houses, cottages, schools and recreational areas) is minimal.

  Take into consideration wind speed, wind direction, temperature inversion, application equipment and sprayer settings.

  Do not apply this product in such a manner as to directly or through drift expose workers or other persons. Unprotected persons must be vacated from the area being treated. Only protected handlers may be in the area during application.

- Aerial application must be removed from the label. For clarification, it is recommended to add the following on all labels:

  Do not apply by air. Use only properly calibrated groundboom equipment as specified by the label.

- In addition, it is recommended that the following statements be added to all MCPB product labels:

  Not for use by homeowners or other uncertified users.

  Do not use in residential areas. Residential areas are defined as sites where bystanders including children may be potentially exposed during or after spraying. This includes around homes, school, parks, playgrounds, playing fields, public buildings or any other areas where the general public including children could be exposed.

Personal Protective Equipment:

- Additional label statements are required regarding personal protective equipment for the purpose of mitigating the risk of exposure to MCPB and in the interest of maintaining consistency between labels:

  Wear chemical-resistant gloves, chemical-resistant footwear, coveralls over long pants and a long-sleeved shirt and when mixing, loading, and applying this product. Pants or coveralls should be worn outside footwear to prevent pooling within boots. Chemical-resistant gloves are not required while operating groundboom sprayers.

Engineering Controls – Closed Cab Application:
Labels must be amended to include the following engineering controls to reduce occupational exposure risk:

> *During groundboom application, use a closed cab that provides both a physical barrier and respiratory protection (i.e dust/mist filtering and/or vapour/gas purification system). The closed cab must have a chemical resistant barrier that totally surrounds the occupant and prevents contact with pesticides outside the cab.*

Limit maximum Kg a.i handled per day:

- USC 13 & 14: Terrestrial Food and Feed Crops
  Groundboom Applications:
  Limit the amount of active ingredient handled to 111 kg a.i. per day
  - *For all crops except seedling grasses, this limit equates to 70 ha at a maximum application rate of 1.594 kg a.i./ha or area treated proportionally adjusted according to specified label rate for the particular crop.*
  - *For seedling grasses, this limit equates to 85 ha at maximum rate of 1.313 kg a.i./ha or area treated proportionally adjusted according to the specified label rate for this crop.*

Post-Application Label Statements – Restricted Entry Intervals (REI):

- Labels must be amended to reflect the REIs that reduce the risk for post-application workers:
  Cereals: *A REI of 1 day after application is required to perform post-application activities in treated areas.*
  Pastures: *A REI of 1 day after application is required to perform post-application activities in treated areas.*
  Seedling Alfalfa: *A REI of 12 hours after application is required to perform post-application activities in treated areas.*
  Seedling Clover: *A REI of 1 day after application is required to perform post-application activities in treated areas.*
  Seedling Grasses: *A REI of 12 hours after application is required to perform post-application activities in treated areas.*
  Peas (succulent/processing): *A REI of 1 day after application is required to perform post-application activities in treated areas.*
  Field Corn: *A REI of 15 days (scouting) and 23 days (irrigation) after application is required to perform post-application activities in treated areas.*

Statements reducing dietary exposure:

- When used on barley, oats, rye, wheat, field corn, peas, pastures and seedling grasses:

> *Do not permit lactating dairy animals to graze fields within 7 days after application.*
> *Do not harvest forage or cut hay within 7 days after application.*
> *Withdraw meat animals from treated fields at least 3 days before slaughter.*

- When used on seedling clover:

  Do not permit lactating dairy animals to graze fields within 30 days after application,
  Do not harvest forage or cut hay within 30 days after application,
  Withdraw meat animals from treated fields at least 3 days before slaughter.

- Plant back interval (PBI):

  A minimum rotational crop plant back interval of 12 months must be observed for all crops other than those registered for use with MCPA or MCPB.

C) <u>Label Changes Relating to Environment</u>

*** Note that aerial application is proposed for phase out based on health concerns. As such, the label changes relating to aerial application may no longer apply pending the final re-evaluation decision.**

<u>All products</u>

Add to **ENVIRONMENTAL HAZARDS:**

Toxic to aquatic organisms, birds and small wild animals.

TOXIC to non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.

<u>For Commercial products</u>

Surface runoff

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.

Leaching

The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow.

Add to **DIRECTIONS FOR USE:**

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 65% of the wing- or rotorspan.

Buffer zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of application	**Crop**		**Buffer Zones (metres) Required for the Protection of:**		
			Aquatic Habitat of Depths:		**Terrestrial habitat**
			Less than 1 m	**Greater than 1 m**	
Field sprayer	Peas, barley, field corn, oats, rye, seedling clover, wheat (spring and durum), seedling grasses, pasture and seedling alfalfa for seed		1	0	3*
Aerial	Barley, oats, rye, wheat (spring and durum) and pasture	Fixed wing	1	0	175
		Rotary wing	1	0	125

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy, the labelled buffer zone can be reduced by 30%.

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners.

D) <u>Label Changes Relating to Value</u>

Label revision for PCP Registration Number 5937:

Under **DIRECTIONS FOR USE**: CROPS – TIMES AND RATES OF APPLICATION:

1. Under APPLICATION RATE, second line to third line which reads "DO NOT exceed 4.25 L/ha" must be revised to read "DO NOT exceed 3.87 L/ha".

2. Under SUSCEPTIBILITY OF WEED TO TROPOTOX SELECTIVE WEEDKILLER LIQUID HERBICIDE:
   a) Under SUSCEPTIBLE WEEDS, first line which reads "USE 3.5 – 4.25 L/ha" must be revised to read "USE 3.5 – 3.87 L/ha".
   b) Under MODERATELY SUSCEPTIBLE WEEDS: "USE 4.25 L/ha" must be revised to read "USE 3.87 L/ha".
   c) Under PERENNIALS:

      SUSCEPTIBLE WEEDS: "USE 4.25 L/ha" must be revised to read "USE 3.87 L/ha".
      MODERATELY SUSCEPTIBLE WEEDS: "USE 4.25 L/ha" must be revised to read "USE 3.87 L/ha".

Label revision for PCP Registration Numbers 24336 and 26488:

1. For use on seedling alfalfa, specify the allowable application rate to be 2.75 to 4.25 L/ha.

References

A) Applicant Supplied Information

PMRA Document Number	Reference
1263063	2000, MCPB (Pure Grade) Physico-Chemical Properties, DACO: 2.13.2,2.14.1,2.14.10,2.14.11,2.14.12,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7,2.14.8,2.14.9 CBI
1202356	TOX (SHORT TERM) - SUMMARIES, DACO: 4.1
1208274	LONG TERM STUDIES- SUMMARIES, DACO: 4.1
1208277	SPECIAL STUDIES- SUMMARIES, DACO: 4.1
1208284	TOXICOLOGY- SUMMARIES, DACO: 4.1
1223469	TOXICOLOGY SUMMARIES, DACO: 4.1
1223470	TOXICOLOGY SUMMARIES, DACO: 4.1
1223499	LONG TERM - SUMMARIES, DACO: 4.1
1246914	MCPA - TOX-SHORT-TERM STUDIES - SUMMARY, DACO: 4.1
1246922	MCPA - SPECIAL STUDIES TOX SUMMARY, DACO: 4.1
1181554	SUMMARIES, ACID, 2-EHE AND DMAS, TOXICOLOGY, METABOLISM, RESIDUES, ENVIRONMENTAL CHEMISTRY AND FATE, ENVIRONMENTAL TOXICOLOGY, JUNE 7, 1996 (COMBINED.CAN) [MCPA INDUSTRY TASK FORCE], DACO: 4.1,6.2,6.3,7.1,8.1,9.1
1086231	2003, MCPB: Acute Oral Toxicity in the Rat - Up and Down Procedure, DACO: 4.2.1
1550798	1985, Acute Oral Toxicity to Rats of MCPB Technical Acid, DACO: 4.2.1
1550916	1995, MCPB Na 400 g/l - Acute Oral Toxicity to the Rat, DACO: 4.2.1
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1550799	1985, Acute Dermal Toxicity to Rats of MCPB Technical Acid, DACO: 4.2.2
1550907	1995, MCPB Na 400 g/l - Acute Dermal Toxicity to the Rat, DACO: 4.2.2

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1086234 2003, MCPB 400 g/l (as sodium salt) Solution: Acute Inhalation Toxicity (Nose Only) Study in the Rat, DACO: 4.2.3

1550803 2007, Waiver Request: Rationale Document for Requesting a Waiver for Acute Inhalation Toxicity (Data Requirement 870.1300) MCPB Sodium Salt (EPA Reg. No. 15440-38) in response to Generic and Product Specific Data Call-In Notice dated March 6, 2007, DACO: 4.2.3

1550804 1985, MCPB (Technical Acid) Acute Inhalation Toxicity Study in Rats 4-Hour Exposure, DACO: 4.2.3

1086235 2003, MCPB: Acute Eye Irritation in the Rabbit, DACO: 4.2.4

1550800 1985, Irritant Effects on the Rabbit Eye of MCPB Technical Acid, DACO: 4.2.4

1550923 1995, MCPB Na 400 g/l - Eye Irritation to the Rabbit, DACO: 4.2.4

1086236 2003, MCPB: Acute Dermal Irritation in the Rabbit;, DACO: 4.2.5

1550801 1984, Irritant Effects on Rabbit Skin on MCPB Technical Acid, DACO: 4.2.5

1550909 2007, MCPB: Acute Dermal Irritation in the Rabbit, DACO: 4.2.5

1550918 1995, MCPB Na 400 g/l - Skin Irritation to the Rabbit, DACO: 4.2.5

1086237 2003, MCPB: Skin Sensitisation in the Guinea Pig (Buehler Method), DACO: 4.2.6

1550802 1985, Delayed Contact Hypersensitivity in the Guinea Pig with MCPB Technical Acid, DACO: 4.2.6

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1223489 3-MONTH DIETARY ADMIN - RATS MCPA ACID TECH, DACO: 4.3.1

1223490 3-MONTH DIETARY ADMIN - RATS MCPA, DACO: 4.3.1

1223491 13 WEEK DIETARY/ORAL ADMIN - DOGS - MCPA, DACO: 4.3.1

1223492 13 WEEK DIETARY ADMIN - DOGS - MCPA, DACO: 4.3.1

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1246920 MCPA - DOG STUDY - 12 MO ADMIN - INTERIM REPORT - AFTER 6 MO ADMIN, DACO: 4.3.1

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1550912 1993, Range-Finding Dietary Toxicity Study with MCPB in Rats, DACO: 4.3.1

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1394646 1978, Range-Finding (4-Week) Toxicity Study with MCPA in Beagle Dogs. Final Report., DACO: 4.3.2

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1394653 1992, Twenty-One Day Dermal Toxicity Study in the Rabbit with MCPA Acid, DACO: 4.3.5

1394655 1993, 21-Day Dermal Toxicity Data (Additional): Determination of Physico-Chemical Properties of MCPA Technical Acid, DACO: 4.3.5

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