RVD2008-20

Re-evaluation Decision

(4-Chloro-2-methylphenoxy)acetic Acid [MCPA]

(publié aussi en français)

22 May 2008

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

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ISBN: 978-0-662-48804-0 (978-0-662-48805-7)
Catalogue number: H113-28/2008-20E (H113-28/2008-20E-PDF)

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Overview

Re-evaluation Decision for MCPA

After a thorough re-evaluation of the herbicide (4-chloro-2-methylphenoxy)acetic acid [MCPA], Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has decided to allow continued registration of certain products containing MCPA for sale and use in Canada.

- The majority of products containing MCPA do not pose unacceptable risks to human health or the environment. They also have value for lawn and turf, agriculture, forestry and industrial uses when used according to the label directions proposed in previous consultation documents. As a condition of the continued registration of these MCPA products, new risk-reduction measures must be included on the labels. In addition, registrants must submit additional confirmatory scientific information, identified in this document.

- Products containing the diethanolamine (DEA) form of MCPA have been phased out as there was a lack of adequate data for assessment.

The regulatory approach regarding the re-evaluation of MCPA was proposed in two consultation documents.[1]

- Proposed Acceptability for Continuing Registration PACR2006-05, *Re-evaluation of the Lawn and Turf Uses of the Herbicide (4-Chloro-2-methylphenoxy)acetic acid [MCPA]*
- Proposed Re-evaluation Decision PRVD2007-01, *The Agricultural, Forestry and Industrial Site Uses of the Herbicide (4-Chloro-2-methylphenoxy)acetic acid [MCPA]*

This Re-evaluation Decision document[2] describes this stage of the PMRA's re-evaluation of MCPA and summarizes the Agency's decision and the reasons for it. Appendix I includes a summary of comments received during the consultation process and the PMRA's response to these comments. This decision is consistent with the proposed re-evaluation decisions stated in PACR2006-05 and PRVD2007-01. To comply with this decision, registrants of products containing MCPA will be informed of the specific requirements affecting their product registrations and of the regulatory options available to them.

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

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

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

generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration.[3] The Act also requires that products have value[4] 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 segments of the population 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 when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

What Is MCPA?

MCPA is a selective systemic phenoxy herbicide that mimics the plant growth regulator indole-3-acetic acid (also known as auxin). It is registered for postemergent control of broadleaf weeds and woody plants. Use is permitted on fine turf, forests and woodlots (spruce seedlings for reforestation), terrestrial feed crops (canary seed/canary grass/annual canary grass, seedling and established legumes, seedling and established grasses for hay, forage or seed production, pastures and rangelands), terrestrial food crops (asparagus, field, canning or processing peas, and sweet corn), terrestrial food and feed crops (flax, barley, oats, rye, wheat, cereals underseeded with legumes, field corn, summer fallow and stubble fields), industrial oil seed and fibre crops (flax), and industrial and non-food sites (non-crop areas). MCPA is formulated as a solution or emulsifiable concentrate/emulsion. It can be applied by ground equipment or by air.

Health Considerations

Can Approved Uses of MCPA Affect Human Health?

MCPA is unlikely to affect your health when used according to the revised label directions. Additional risk-reductions measures are required on MCPA labels.

Exposure to MCPA may occur through diet (food and water), when handling treated plants, working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing

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

[4] "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."

mothers). Only those uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

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

An overexposure to MCPA may cause severe irritation to the eyes, slurred speech, twitching, jerking, spasms, drooling, low blood pressure and unconsciousness. Additional neurological, developmental and kidney effects occurred during laboratory testing at high doses only; therefore, they would not occur when MCPA products are used according to the label directions. Although there were no signs of cancer in the chronic mouse and rat studies, the rat study did not reach the maximum tolerated dose (MTD); therefore, another study is required.

Because there were some risks of concern based on current uses of MCPA, additional protective measures (product use changes, personal protective equipment and improved work practices) will be included on product labels to further reduce the level of human exposure to MCPA. In addition, specific toxicity information regarding symptoms of overexposure are required in the Toxicological Information section of the product labels (see Measures to Minimize Risk later in this document).

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 (ARfD) on a daily basis, or less than 100% of the acceptable daily intake (ADI) over a lifetime. Exposure to MCPA was estimated from residues in treated crops and drinking water, including the most highly exposed human populations (e.g. infants, children, teenagers, adults and seniors).

Chronic exposure accounted for 37% of the ADI in children 1 to 6 years old and less than 23% of the ADI in the remaining subgroups. The acute exposure evaluated at the 99.9th percentile for females of childbearing age accounted for 3.5% of the ARfD and less than 4.4% for all other segments of the population.

A drinking water level of comparison is the maximum concentration in drinking water that, when considered together with all other sources of exposure, does not exceed a level of concern. The maximum estimates of acute and chronic residues of MCPA in drinking water were 4.2 and 0.26 µg/L. These values are well below the acute and chronic

drinking water level of comparisons for the most sensitive populations, established at 4012 and 75 µg/L, respectively. They are therefore not a health concern.

Residue Definition and Maximum Residue Limits

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 the *Food and Drugs Act* 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.

Currently, there are no specified MRLs for MCPA. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which indicates that pesticide residues in a food commodity must not exceed 0.1 ppm.

In order to accept residue data in support of lowering the postapplication grazing interval, a residue of concern must be established with proper analytical methods for its enforcement. The residue of concern for enforcement is defined as the MCPA per se for animal tissue and as MCPA with its 2-HMCPA metabolite (4-chloro-2-hydroxymethyl-phenoxy)acetic acid for plants. The PMRA will accept studies based on MCPA per se for surveillance and to establish MRLs. Confirmatory analytical methods to establish these residues of concern are required as part of this decision.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern.

Risks to homeowners and their children from contact with treated lawns and turf are not of concern.

Occupational Risks From Handling MCPA

Occupational risks are not of concern.

Risk estimates associated with mixing, loading and applying activities for registered uses are acceptable, provided that products containing MCPA are used according to the label directions and the required mitigation measures are followed. These measures are needed to minimize the potential for exposure, thus protecting worker health and safety.

Postapplication risks are not of concern to workers.

Postapplication occupational risk assessments consider exposures to workers entering treated agricultural, forestry, industrial sites, golf courses and sod farms. Based on the precautions and directions for use on the original product labels reviewed for this re-evaluation, postapplication risks to re-entry workers performing various activities are

generally not of concern provided that products containing MCPA are used according to the label directions and the required mitigation measures are followed.

Environmental Considerations

What Happens When MCPA Is Introduced Into the Environment?

MCPA is toxic to certain terrestrial and aquatic organisms; therefore, additional risk-reduction measures must be observed.

MCPA released into the environment can be found in soil and surface water. There is some evidence that the use of this herbicide may result in groundwater contamination. MCPA residues will not bind to soil or sediment and can be removed by water. Most of the MCPA residues are rapidly degraded by microorganisms.

The use of MCPA poses a concern with regard to the following terrestrial organisms: native and wild plants. It also poses a concern regarding aquatic organisms such as fish, amphibians, aquatic invertebrates and aquatic plants. To reduce exposure of these organisms, it is important that additional risk-reduction measures (e.g. buffer zones) are observed.

Value Considerations

What Is the Value of MCPA?

MCPA is commonly used for broadleaf weed control and is the second most widely used herbicide in Canada based on the amount of active ingredient used. The use of MCPA reduces the economic losses incurred annually by weeds across Canada and is considered a cost-effective herbicide.

MCPA has been recognized as a superior tank-mix partner with other herbicides. These tank mixes control a broader range of weeds compared to products containing only a single active ingredient, resulting in fewer applications, less soil compaction and reduced costs for growers.

MCPA is integral to the management of weed biotypes resistant to other herbicide groups. There is little evidence of weed resistance following years of MCPA use.

Measures to Minimize Risk

The labels of registered pesticide products include specific instructions for use. The directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law.

Risk-reduction measures are being implemented to address potential risks identified in the assessment of all MCPA uses. In addition to the measures on existing MCPA product labels,

these measures are designed to further protect human health and the environment. Registrants will be required to amend their labels to reflect these additional measures.

Additional Key Risk-Reduction Measures

A. The phase-out of products and uses that do not meet current standards for human health risks or risks to the environment

- All products containing the DEA form of MCPA have been discontinued.

B. Label upgrades to further increase protection of human health and the environment, as detailed in Appendix II

- Label statements will more accurately describe the product and its allowed uses.
- For some uses, the maximum application rates of products and/or the number of applications per year have been revised to prevent unnecessary use of MCPA.

Human Health

- The TOXICOLOGICAL INFORMATION section will be updated to provide information about symptoms and treatment for over-exposed individuals.

- A variety of mitigation measures are required to protect mixers, loaders and applicators with the highest potential for exposure. These include additional protective equipment, reductions in quantity and/or concentration of product applied, and use of approved application equipment.

- Workers entering treated sites must use personal protective equipment and observe restricted-entry intervals in some postapplication exposure scenarios.

- Restrictions on grazing and harvesting of forage must be observed to reduce dietary exposure.

Environment

- Product labels are being revised to reduce the release of MCPA into the environment. Labels will have instructions for minimizing the contamination of water by runoff and minimizing accidental spray drift to terrestrial and aquatic sites.

- Labels will also contain statements to protect aquatic and terrestrial habitats that may contain sensitive species. Terrestrial and aquatic buffer zones must be observed. The specific distance depends on the type of spray equipment, the application rate and the water depth.

What Additional Scientific Information Is Being Requested?

The risks and value have been determined to be acceptable if all risk-reduction measures proposed in the consultation documents are followed when using the products accepted for continued registration. To refine the current risk assessment, confirmatory scientific information is being requested from registrants as a result of this re-evaluation. Registrants will be asked to submit this information within specified time frames.

Chemistry

- The results from the analysis of the active ingredient and all impurities present below 0.1% from five recent batches of the technical grade active ingredient.

- An updated Statement Product Specification Form is required for all products to which dimethylamine (DMA) is added during the manufacturing or formulation process. The form must identify the levels of *N*-nitrosodimethylamine (NDMA) in the DMA used. This requirement will ensure that registrants continue to purchase DMA with extremely low levels of microcontaminants.

Human Health

- A long-term oncogenicity study is to be conducted in rats (Wistar) using the form MCPA-2-ethylhexyl ester (MCPA-2-EHE) (Data Code [DACO] 4.4.2). The PMRA has accounted for uncertainties associated with specific studies through the application of additional uncertainty factors for risk assessment.

- Analytical methodologies for monitoring and enforcement are required:
  - a multiresidue method for MCPA surveillance
  - an enforcement analytical method for plants that includes MCPA and 2-HMCPA

Other Information

The relevant test data on which the decision is based are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this decision on MCPA within 60 days from the date of publication of this Re-evaluation Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the PMRA's website (Requesting a Reconsideration of Decision, www.pmra-arla.gc.ca/english/pubreg/reconsideration-e.html), or contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

[5] As per subsection 35(1) of the *Pest Control Products Act.*

List of Abbreviations

2-EHE	2-ethylhexyl ester
ADI	acceptable daily intake
a.e.	acid equivalent
a.i.	active ingredient
ARfD	acute reference dose
ARI	aggregate risk index
bw	body weight
DACO	data code
DEA	diethanolamine
DEEM	Dietary Exposure Evaluation Model
DMA	dimethylamine
DT_{50}	time required for 50% dissipation
EC_{25}	effect concentration 25%
EC_{50}	median effect concentration
F_0	parental generation
F_1	first filial generation
kg	kilogram
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	lowest observed adverse effect level
m	metre
MCPA	(4-chloro-2-methylphenoxy)acetic acid
mg	milligram
NDMA	N-nitrosodimethylamine
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
RQ	risk quotient
TTR	turf transferable residue
UF	uncertainty factor

Appendix I Comments and the PMRA's Responses

The PMRA received comments in response to PACR2006-05 and PRVD2007-01 from a variety of stakeholders, including registrants, non-governmental organizations with interests in human health or the environment, provincial governments, users of MCPA and the general public. Some contained additional data or information for consideration by the PMRA. Some of the comments requested changes of an editorial nature, which have been incorporated into the reviews without further discussion and will not be reiterated in this section. The PMRA has consolidated and summarized the remaining comments received and provides responses below.

The comments have been grouped as indicated below.

1.0 Comments with Respect to Chemistry
2.0 Comments with Respect to Toxicology
3.0 Comments with Respect to Residues and Exposure
4.0 Comments with Respect to Environment
5.0 Comments with Respect to Value

1.0 Comments with Respect to Chemistry

1.1 Comment

The physical and chemical properties of other forms of MCPA should be presented along with the acid form.

Response

Other forms of MCPA (amine salts and mixed sodium and potassium salts) that were covered by PACR2006-05 are not registered as technical grade active ingredient products. Therefore, the physical and chemical properties for the pure forms of these compounds are not available. Amine salts and mixed sodium and potassium salts of MCPA are formed during the formulation process of the end-use products. Consequently, the physical and chemical properties are only available for the formulations and as such are not presented.

1.2 Comment

The NDMA level should not be required to be reported on the specification form.

Response

An updated Statement Product Specification Form is required for all products to which DMA is added during the manufacturing/formulation process. This is to be used as a method of monitoring NDMA content and will ensure that registrants continue to purchase DMA with extremely low levels of microcontaminants.

2.0 Comments with Respect to Toxicology

2.1 Comment

The inhalation median lethal concentrations (LC_{50})s and acute and dermal median lethal doses (LD_{50}s) for each form of MCPA should be reported.

Response

These values can be obtained from individual Material Safety Data Sheets (MSDS) for each product. As stated in the review, the different MCPA technical actives were of low acute dermal and inhalation toxicity (LD_{50} > 2000 mg/kg bw and LC_{50} > 2.0 mg/L) and of slight to moderate acute oral toxicity (LD_{50} between 500 and 2000 mg/kg bw).

2.2 Comment

There were no toxicological studies/assessments for MCPA, mecoprop-p and dicamba mixtures.

Response

Available acute animal toxicity data on these product mixtures indicate lower toxicity values when compared to individual full-strength active ingredients. Herbicide mixtures are more effective for weed control than are higher rates of a single constituent because of their synergistic effect on plant-specific growth regulators.

2.3 Comment

The DEA form of MCPA should be removed from the shelf immediately.

Response

The DEA form of MCPA was not supported by the MCPA Task Force III, which consists of technical registrants of MCPA, and was phased out because adequate data were not available. All affected products have been discontinued by the registrants.

2.4 Comment

The studies characterizing the oncogenic and neurotoxic effects are insufficient.

Response

The PMRA reviewed acute and short-term neurotoxicity studies for each form of MCPA. These studies demonstrated that neurotoxic effects were only evident at very high doses in excess of renal saturation. Sufficient margins of safety (MOS) between these doses and potential human exposure levels were established in the risk assessment to ensure such effects were highly unlikely to occur in humans, including children. Additional neurotoxicity studies, including a developmental neurotoxicity study, are not required.

Potential oncogenicity issues are addressed under Comments 2.6 and 2.13.

2.5 Comment

The potential effects on the endocrine system will eventually have to be analyzed.

Response
For human health assessment, the potential for a given pesticide to elicit endocrine-modulating (hormonal) effects is currently assessed from animal studies such as multigeneration reproductive toxicity assays and chronic toxicity/carcinogenicity assays. These studies form part of the data requirements for pesticide registration and have the potential to reveal numerous endpoints that may be directly or indirectly related to endocrine disruption. Based on current standards, no evidence for effects on the endocrine system were noted in the MCPA database (refer to Comment 2.11).

2.6 Comment
Would it not be wiser to wait for the new studies than to indicate that the PMRA has concluded that the lawn and turf use of MCPA does not pose unacceptable risk to human health?

Response
Currently, the PMRA requires the submission of a new chronic rat study. The current rat study did not dose high enough to sufficiently challenge the animals for a meaningful cancer assessment. However, the current study did not show any carcinogenicity up to the highest dose tested (17.5 mg/kg bw/day), the chronic mouse study did not show any evidence of cancer, and all in vivo genotoxicity studies were negative. In addition, the PMRA included an additional 3× safety factor in the chronic risk assessment, since the chronic rat study did not reach an MTD. This creates a sufficient margin of safety (>1400×) to the no observed adverse effect level (NOAEL) of 17.5 mg/kg bw/day. In other words, the current acceptable daily intake is 1400 times lower than the NOAEL of 17.5 mg/kg bw/day. Even without the new study, in light of the available data, the PMRA considers the cancer risk to be low. Therefore, the requested study would be used in the weight of evidence to confirm this finding.

2.7 Comment
With respect to genotoxicity studies, the mammalian in vitro lymphocyte assays were “positive” at dose levels that were also cytotoxic. Thus, MCPA is not genotoxic.

Response
The “positive” results were restricted to high doses, but only the acid form of MCPA was cytotoxic as well. All in vivo assays were negative .The PMRA will conduct its weight-of-evidence examination of genotoxicity following receipt and review of a new two-year rat study using MCPA-2-EHE.

2.8 Comment
The high doses and relative non-specificity of the neurological signs in the acute neurotoxicity tests most likely reflect poor general condition of these rats after a very high dose of compound rather than a specific neurotoxic effect. Thus, the adoption of this endpoint is questionable and an additional 3× safety factor to account for “use of LOAEL” (lowest observed adverse effect level) is unwarranted.

Response
Acute neurotoxicity studies were submitted for MCPA-acid, DMA and 2-EHE. The acid study set the NOAEL at 150 mg/kg bw, based on increased ataxia, abdominal tension and decreased body weight at 300 mg/kg bw. The MCPA DMA study did not identify a NOAEL because ataxia was noted at the lowest dose tested (146 mg/kg bw). Similar results were noted for MCPA 2-EHE. At the lowest dose tested (167 mg/kg bw), increased ataxia, abdominal tension, decreased open field activity and righting reflex were noted. Since ataxia was evident with all three forms of MCPA after a single dose, the PMRA defaulted to the lowest effect level for the acute endpoint selection. Regardless of whether the above clinical effects are related to neurotoxicity or systemic toxicity, they are occurring after one dose and are indicative of an acute exposure. Because a NOAEL could not be established for the MCPA-DMA and 2-EHE studies, and since current PMRA policy is to add an uncertainty factor when a LOAEL is used for endpoint selection, the additional 3× factor for acute exposure in the general population scenario will be retained.

2.9 Comment
The rat study should be used for the "Short-term 8- to 30-day dermal" endpoint selection, not the rabbit study.

Response
This comment was made following the MCPA turf assessment. The PMRA agreed and subsequently modified the endpoint selection for the assessment of agricultural, forestry and industrial uses.

2.10 Comment
The fetal effects (rat developmental study) are only seen after several days of dosing at levels where the threshold for renal clearance was exceeded for at least part of the day, such that there was "carryover" into the circulation for the subsequent day. Therefore, the extra 3× safety factor for developmental effects is unwarranted.

Response
The fetal effects seen at 120 mg/kg bw/day in the 2-EHE developmental rat study included decreased viable litter size, increased postimplantation loss, early resorptions, hydrocephaly and bent limbs. Any of these effects can occur after one exposure. Furthermore, the dams did not show overt signs of renal saturation at 120 mg/kg bw/day after nine days of exposure. Although the dams did have decreased body weight, the PMRA considers the above-mentioned fetal effects to be a qualitative sensitivity. Therefore, the 3× safety factor for fetal sensitivity will be retained in the acute exposure scenario for females 13 years and older.

2.11 Comment
Clarification is requested regarding the interpretation that testicular effects are seen in all species at higher doses.

Response
The PMRA maintains that testicular effects are seen in all species at high dose levels that exceed renal clearance. Species include the mouse, rat and dog. Testicular effects are seen at lower doses in the dog. However, it is acknowledged that the lower dose levels in the dog also exceeded renal saturation and that the dog is not a good indicator species for the human health risk assessment. With the mouse and rat, the testicular effects occur well above the NOAELs used in the various endpoint selections, creating an adequate margin of safety and making effects in humans very unlikely. Also, since the testicular effects occur at doses that exceed renal clearance, they were not considered to be directly related to an endocrine effect.

2.12 Comment

Comments pertaining to the rat reproduction study.

- There is no offspring sensitivity indicated in the study, as the PMRA suggests.
- Although the MTD was not reached, the highest dose was close to the MTD.
- Other countries have accepted the reproduction study as sufficient; a new study is not needed.
- One-generation studies with MCPA-acid and 2-EHE were submitted.

Response
The two-generation reproduction study in rats (1986) tested MCPA acid at dose levels of 0, 2.5, 7.5 and 22.5 mg/kg bw/day. Maternal animals were not dosed to the MTD, and thus did not demonstrate any toxicity. In the absence of maternal toxicity, both generations of pups had decreased body weight and body-weight gain on postnatal day 21 with a borderline effect on postnatal day 14, demonstrating the potential for increased sensitivity of the young. Thus, in PACR2006-05, the PMRA requested a new two-generation reproduction study.

Subsequent to the PMRA's review of MCPA for lawn and turf, the MCPA Task Force III submitted one-generation rat studies for MCPA-acid and 2-EHE. For each study, groups of Wistar-derived rats (12/sex/dose) were fed diets containing MCPA acid or acid equivalent at dose levels higher than the original study. Animals were dosed for 10 weeks, mated and allowed to rear the ensuing litters. Dietary concentrations were decreased to 65% of the initial concentrations from day 1 postpartum and fed throughout the postpartum period. On day 29 postpartum, 10 first filial generation (F_1) males and 10 F_1 females per group were selected and retained for two weeks. They were fed diets containing the pre-mating dietary concentrations.

As these studies were only range-finding studies and the PMRA did not support decreasing the dietary concentration to 65% of the initial dietary concentration, the PMRA considered the studies supplemental and defaulted to the lowest achievable dose levels, which were equivalent to 36, 57 and 75 mg/kg bw/day. Since the PMRA was concerned with the lack of MTD and decreased pup body weight in the original reproduction study, these concerns were its primary focus in assessing these studies.

The parental generation (F_0) adult males, for both MCPA-acid and 2-EHE range-finding studies, had a borderline effect on body weight and F_0 females had increased kidney weights (absolute and relative) at all dose levels. Body weight in the pups was affected, but not until postnatal days 29 to 43 (the three-week observation period for the F_1 adults). F_1 adults also had decreased liver and gonad weights (primarily high-dose effects with the acid, and mid- to high-dose effects with

the 2-EHE). Although these effects on organ weights cannot be substantiated with clinical chemistry or detailed histology (limitations of range-finding studies), the effect on body weight does indicate that the MTD was likely reached in the F_1 adults. Also, both studies showed that pup body weight was not adversely affected until after weaning, indicating there is no sensitivity of the young.

Therefore, based on the results of these two reproduction range-finding studies, the PMRA has reassessed the parental and reproduction NOAELs to be 22.5 mg/kg bw, the highest dose tested in the original reproduction study. A new rat reproduction study is no longer required and PRVD2007-01 reflects there is no sensitivity of the young in the rat reproduction study.

2.13 Comment

Comments relating to the chronic rat study (MCPA acid) and endpoint selection for the ADI used in the assessment:

- A new study is unnecessary. The current one is scientifically adequate for the purposes of evaluating potential oncogenic effects of MCPA.
- Renal saturation occurs at levels only slightly above the high dose in the existing study.
- If a new study is conducted, there is no reason why it has to be conducted with the ester form of MCPA.
- Use of a 90-day study *and* the application of an additional factor to reflect the lack of MTD is illogical for the calculation of the ADI.

Response

The primary objective of a cancer study is to challenge the animals sufficiently to identify oncogenic potential. Although the chronic mouse study showed no evidence of oncogenicity, the highest dose tested in the current rat study (17.5 mg/kg bw/day) failed to elicit any systemic toxicity. Subsequent to PACR2006-05, the MCPA Task Force III submitted a number of toxicokinetic studies with the acid form, which showed that renal saturation in the rat occurred at about 80 mg/kg bw/day. Typically with phenoxy herbicides, systemic toxicity is observed at dose levels near and above renal saturation. Thus, the highest dose in the chronic rat study is about four times lower than any dose causing renal saturation in the rat. This supports the PMRA's claim that the MTD was not reached in the chronic study and a new study is required to adequately test for oncogenic potential.

Although the different forms of MCPA are considered toxicologically equivalent, the toxicity of the ester form was slightly more severe (qualitative but not quantitative). Although this did not impact endpoint selection in the current assessment, utilizing this form will help to characterize any differences between the acid and ester forms following chronic dosing.

With respect to the use of the 90-day rat study to calculate the ADI, the PMRA recognizes that the kidney effects noted with MCPA acid in the 90-day dietary rat study at 10.9 mg/kg bw/day were not apparent in the two-year rat study with MCPA acid at 17.5 mg/kg bw/day. However, the 90-day rat neurotoxicity studies (with MCPA-acid, DMA and 2-EHE) also had various effects at 34/36 mg/kg bw/day (NOAEL of 3.3 mg/kg bw/day). In particular, increased creatinine (females), water consumption, decreased bw/bwg and motor activity were noted in the 90-day MCPA-2-EHE neurotoxicity study.

Based on the effects observed in the 2-EHE neurotoxicity study, which were qualitatively more severe than in the acid neurotoxicity study, and the lack of a chronic study, a new two-year rat study with MCPA-2-EHE is required to characterize any potential oncogenic and systemic toxicity.

The application of an extra 3× uncertainty factor is applied for the lack of an MTD in the chronic rat study. The ADI calculated is more than 1400 times lower than the NOAEL of 17.5 mg/kg bw/day established in the current chronic rat study. The PMRA will reassess the ADI and any conservatism in endpoint selection/safety factors applied after the submission and evaluation of the new chronic rat study.

3.0 Comments with Respect to Residues and Exposure

3.1 Comment

It is not clear how the value of 7.3% for transferable residues was derived in the PACR2006-05.

Response

The 7.3% value is the arithmetic mean of the peak MCPA turf transferable residues (TTR) (presented as the percentage of active ingredient applied) for each site and formulation from all three phases of the submitted turf transferable residue study.

3.2 Comment

It should be recognized that residue decline for MCPA use on grass is rapid and that of transferable residues even more rapid, such that after 48 hours these are generally negligible. The use of a seven-day average TTR value under these circumstances is questionable, especially for a compound where excretion is known to be rapid.

Response

At two of the three sites where MCPA residues were measured in the TTR study (North Carolina and California), residues of MCPA above the limit of quantification were found up to seven days after application. As such, it was considered appropriate to use a seven-day average TTR value to estimate short-term exposure to MCPA from treated turf.

3.3 Comment

The PMRA recommends not applying more than two broadcast applications per season to turf (not including spot treatments); however, this statement does not appear on the label.

Response

All product labels will require the statement that no more than two broadcast applications should be made per season (not including spot treatments).

3.4 Comment

As a mitigation measure, the label should include a statement delaying re-entry into treated areas for 24 hours before people may contact treated turf.

Response
A restricted-entry interval is required for workers transplanting and harvesting treated turf on sod farms only. The risk assessment for MCPA indicates that risk for all other populations contacting treated turf is acceptable on the day of application, once residues have dried. As such, a restricted-entry interval (REI) is not required for these populations.

3.5 Comment
The method for deriving a dermal absorption factor of 19% should be explained. Based on a review of various studies, a dermal absorption factor of 7% would be more appropriate.
(Note that an additional rationale was submitted after the comment period and suggested that the dermal absorption factor be changed to 8%, based on a review of existing studies.)

Response
PMRA's derivation of the dermal absorption factor relied on the same studies as referred to by the MCPA Task Force III. However, in determining the dermal absorption factor, the skin bound residues (12% absorption of applied dose) were included with the systemically absorbed test material (7% of the applied dose) as the fate of these skin bound residues is uncertain. The PMRA also considered the additional rationale sent by the MCPA Task Force III. However, the Agency did not find this rationale to be adequate in supporting the use of an 8% dermal absorption factor. The PMRA will continue to include the skin bound residues in deriving the dermal absorption factor for MCPA until there is evidence showing that skin bound residues are not absorbed systemically over time. Should the MCPA Task Force III wish to submit new scientific studies in support of a reduced dermal absorption value, the PMRA will review these studies in the future.

3.6 Comment
Hand detasseling is not part of the postapplication activities as evaluated by the PMRA in the postapplication risk assessment for field and sweet corn.

Response
After verification of agricultural practices for field and sweet corn, the PMRA has found that hand detasseling is not common practice. It has therefore been removed from the postapplication risk assessment for the agricultural uses of MCPA.

3.7 Comment
A new study, *Magnitude of the Residues of MCPA in Dairy Cow Milk and Tissues*, ABC Study # 49737 (Koch 2007, PMRA#1394727), was submitted in support of reducing postapplication restrictions for harvest forage and cut hay from 30 to 7 days.

Response
This study (Koch 2007) examined exposure of lactating cows to residues from hay. Evidence is adequate to reduce the existing preharvest interval from 30 to seven days. The required label amendments have been revised accordingly (Appendix II).

4.0 Comments with Respect to Environment

4.1 Comment

How can any enforcement activity or court uphold a buffer that can be calculated each and every time a farmer or applicator enters a field to apply a product?

Response

Buffer zones can be enforced legally as they are specified on MCPA labels.

4.2 Comment

How does one apply buffer zones to temporary water?

Response

Buffer zones are not required for temporary pools of water.

4.3 Comment

A five-metre buffer zone from sensitive terrestrial habitat is quite large. It is unclear whether windbreaks are considered part of sensitive terrestrial habitats. Windbreaks are often within a five-metre distance from the edge of a crop. Many Ontario growers have planted windbreaks to help reduce soil erosion and wind damage to crops, improve pesticide applications by reducing wind speed and catch drifting pesticides. This issue may be better addressed with a label statement alerting pesticide applicators that MCPA may be injurious to sensitive terrestrial habitats, including windbreaks, and should be avoided.

Response

The five-metre buffer zone was calculated based on the crop toxicity data provided to the PMRA by the registrant and on the application rate specified on the label. Toxicity data on non-crop species may be more relevant for addressing this. Buffer zones are calculated with the use of a model and represent the setback necessary for the protection of sensitive terrestrial habitat.

The usefulness of windbreaks is well recognized. However, they are considered to be sensitive terrestrial habitats. A sensitive terrestrial area is defined as any area within or adjacent to a spray area that consists of vegetation at risk such as, but not limited to, a forest, shelterbelt, meadow, hedgerow or riparian vegetation.

4.4 Comment

The size of the buffer zones will cause considerable difficulty for many farmers. This product has been used for over 60 years with no evidence of appreciable non-target impact. The buffer zones proposed in PRVD2007-01 are not practical for the application of MCPA to cereals. Propose buffer zones for MCPA to determine if crop-specific and/or rate-specific buffer zones or other approaches offer more appropriate solutions. A separate buffer zone table for cereals should be added to reflect the rate used on these crops.

Response
With a view to reduce the buffer zones, the risk assessment of MCPA has been refined with the use of more up-to-date methods. The proposal that buffer zones for MCPA should be crop- and/or rate-specific will be considered. However, when there are several applications during the season, a cumulative application rate based on half-life of MCPA is used in the calculation of buffer zones. A separate buffer zone table for cereals that reflects the rate and number of applications per season may be considered in the future.

4.5 Comment
While there is low potential for MCPA acid to bioaccumulate, the octanol–water partition coefficient should be corrected. The pH 5 value used in the EU is 0.28 to 0.59, which is closer to the expected value for a compound with a dissociation constant (p*K*a) similar to MCPA (Bailey and Hopkins, 1987). The following values are more appropriate: pH 7 (−0.81 to −0.71); pH 9 (−1.07 to −0.88) for 0.01 and 0.001 molar solutions, respectively.

Response
The values for the octanol– water partition coefficient that were provided by the MCPA Task Force III will be used to replace the values currently in PRVD2007-01. The new values also indicate that MCPA has a low potential to bioaccumulate.

4.6 Comment
The rapid conversion of MCPA-2-EHE to MCPA observed in an adsorption/desorption study conducted with soils sterilized by gamma radiation (Sarf 2007, ABC Labs 49703, *Determination of Adsorption and Desorption to Soils for MCPA-2-EHE*; MRID #47075204) indicates the process is a soil surface phenomenon and is not microbially mediated.

Response
The reference to the new adsorption/desorption study with sterilized soils is noted. However, the description of transformation of MCPA-2-EHE in PRVD2007-01 was in non-sterilized anaerobic soil.

4.7 Comment
The hydrolysis timing statements are applicable only to sterile water. There are new data that show much more rapid hydrolysis in natural waters (Stewart 2006, Brixham BL8277B and Harper 2006, Huntingdon Life Sciences TFT 0009/054012, *MCPA-2-EHE Determination of Aqueous Stability in Distilled and River Water*).

Response
The reference to the new data is noted. The protocol for hydrolysis studies requires the use of sterile and buffered water because hydrolysis is an abiotic transformation process. Its rate is affected by the pH of the water. In natural waters, there may be other transformation processes taking place.

4.8 Comment

Studies on the effects on aquatic organisms were performed with MCPA-2-EHE used at concentrations in excess of the water solubility (a more accurate water solubility has been performed recently and is included in the reports from Brixham and HLS, referred to in Comment 4.7). A detailed critique of each of the ester studies was made and the only safe conclusion that can be drawn from any of these studies is that MCPA-2-EHE has no effect at the limit of solubility. As the PEC should not exceed the water solubility, then by definition all risk quotients (RQs) must be less than or equal to one.

Response

The reports from Brixham and HLS indicated that the water solubility of MCPA-2-EHE was 57 µg/L at pH 7 buffer and 110 µg/L at pH 9 buffer. It also ranged from 83 to 150 µg/L in the ecotoxicological test media used for algae, *Lemna* and *Daphnia*. In the ecotoxicological test media, there was rapid hydrolysis to MCPA acid, which suggested that test organisms would have been exposed to both the ester and acid. Therefore, a revision will appear in the Evaluation Report to indicate that the median effect concentration (EC_{50}) values of 0.13 to 0.17 mg a.e./L reflect the toxicity of both the ester and acid.

4.9 Comment

There is a new 14-day study with *Lemna gibba* that shows that the EC_{50} was 1.5 mg a.e./L. This study is preferred over previous studies as it is fully guideline compliant and the concentration of test substance was maintained at a constant level throughout the study. *(A document evaluating the various Lemna studies available with MCPA was submitted.)*

Response

PRVD2007-01 states that "MCPA-DMA was less toxic to *L. gibba* with an EC_{50} of 0.124 mg a.e./L." The report provided a review of a number of studies on the effect of MCPA on *Lemna*. It pointed out that the study that determined an EC_{50} of 0.124 mg a.e./L was a static test and was deficient because there was a 60 to 70% loss of test substance during the study. This study was previously reviewed by the PMRA and deemed acceptable. However, there were other studies considered unacceptable by the MCPA Task Force III in which the toxicity endpoints were similar to those in which the EC_{50} was 0.124 mg a.e./L.

4.10 Comment

The RQs will be substantially reduced by using the data from the new study submitted.

Response

The RQ values for freshwater vascular plants were 6.4 to 7.5 for ground sprayers and 64 to 75 for aerial application. The aquatic risk assessment will be updated according to current methods, which are less conservative. However, the PMRA will maintain the selection of aquatic toxicity endpoints that were deemed acceptable during the review of MCPA.

4.11 Comment

The statement of high acute risk for marine algae is presumably based on a *Skeletonema* study, although this is not apparent from the evaluation. A critique of studies performed at this time compared to subsequent results from several laboratories in different concentrations has been submitted. A more recent guideline-compliant study showed an EC_{50} of 34 mg/L. Use of this value will give a significantly reduced RQ.

Response

The aquatic risk assessment for marine algae was based on *Skeletonema costatum* with a 96-hour EC_{50} of 0.11 mg a.e./L. The more recent study is reported to have an EC_{50} of 34 mg/L. It should be noted that the earlier study with *Skeletonema costatum* was deemed acceptable during the review stage for MCPA and that the most sensitive species is considered in the aquatic risk assessment.

4.12 Comment

The buffer zones based on the cumulative application rates seem unreasonable. The interval between repeat applications is such that the vast majority of any residue will have been degraded in the environment before the second application is made. This degradation will include drift. If susceptible plants have absorbed drift from the first application, then experiments have shown that there will be significant metabolic degradation/growth dilution prior to the second application. Thus, these values should be reduced to reflect the above. A conservative value might be 105 or 110% of the maximum instantaneous application rate.

Response

The cumulative application rate is calculated using the maximum single application rate, the number of applications per season and the rate of transformation of MCPA in environmental compartments (i.e. DT_{50} in soil, water or on food sources).

4.13 Comment

The no observed effect concentration (NOEC) for *Skeletonema* is not applicable in aquatic buffer zones. In view of the stability of the ester in the various media, there is only a need to use the MCPA acid/DMA data. Here the NOEC values are much higher (*Skeletonema*, 11.6 mg/L , Palmer 1999) and for *Lemna* either 0.254 mg/L (*L. minor*, Mattock 1998), 16.2 mg/L (*L. gibba*, Drottar 1999), or 10.0 mg/L (*L. gibba*, Moore 2000).

Response

The aquatic risk assessment will be adjusted based on the current methods where the endpoint used for algae is half the LC_{50} and not the NOEC.

4.14 Comment

PRVD2007-01 indicates that the buffer zones for the protection of terrestrial habitats are based on the cumulative application rates of 2.89 and 3.39 kg a.e./ha (for crops and non-crops, respectively). Cumulative application rates of 2.49 and 2.92 kg a.e./ha are used for protection of aquatic organisms (also defined as for crops and non-crops, respectively). The reason for the difference between the cumulative application rates is uncertain if they are both based on application rates for crops and non-crops. In addition, due to the rapid dissipation of residues following the initial application and any potential reapplication, it is not believed that the use of cumulative application rates is appropriate.

Response

The difference between the cumulative application rates for crops and non-crops is due to the significant difference in application rates for crops versus non-crops. Cumulative application rates are calculated based on the MCPA half-life and duration between applications.

4.15 Comment

The proposed cumulative application rate proposed by the MCPA Task Force III for cereal grain uses was 875 g a.e./ha. The lowest cumulative rate used by the PMRA (2.49 kg a.e./ha) to define the buffer zones is more than 2.8 times the proposed rate for the largest proposed use of the product (cereal grains).

Response

The cumulative application rate is calculated using the maximum single application rate, the number of applications per season and the rate of transformation of MCPA in environmental compartments (i.e. the time required for 50% dissipation (DT_{50}) in soil, in water or on food sources). In field crops, the maximum single application rate of MCPA is 1875 g a.e./ha, and this rate may be applied twice per season. For non-crop sites, the maximum single application rate of MCPA is 2200 g a.e./ha, and this rate may be applied up to twice per season.

4.16 Comment

The complexity of the proposed buffer zone table in PRVD2007-01, in the case of the crop uses categorized by application technique and crop, is inappropriate. Categorization by application technique and rate may be more appropriate to avoid the variable between crop determinations of appropriate buffer zones, particularly noticeable with respect to terrestrial habitats using aerial application methods. The presentation of this buffer zone table in its current form as a label component would simply frustrate users. Lack of clear definitions of sensitive terrestrial habitats would similarly confuse and frustrate users. It is appreciated that the PMRA acknowledges that buffer zones to adjacent rangeland and pasture would not be required for agricultural crop applications. However, it may be more appropriate to provide general guidance on avoiding drift to non-target areas. Several of the sensitive terrestrial habitat examples listed are registered use sites for MCPA products, and may well be the targeted area for an MCPA application at a different time. Whether an adjacent area to an MCPA application could be considered “sensitive” is often a subjective determination by the land manager, influenced by his management intentions for an adjacent area, the avoidance of conflict with neighbouring landowners or managers, and expert guidance on the value of species that could be damaged by spray drift to a non-target area. Rather than list a series of land use types (i.e. grasslands, woodlots, shrublands, etc.), more general guidance to users on avoiding drift to non-target areas

is advised. There is concern that implementation of establishing buffer zones for MCPA products is premature, considering the PMRA has not finalized its Buffer Zone Strategy documents and captured the input from all concerned stakeholders. If strictly observed, the proposed buffer zones (particularly for aerial application) will render the application technique virtually useless in many locales.

It is recommended that in the absence of refinement of the above points, the proposed label statements regarding buffer zones be deleted. Any introduction of label statements related to buffer zones should only take place after finalization of the Buffer Zone Strategy, and in conjunction with similar introductions for all other pesticides.

Response
Buffer zone calculations for specific crops are based on their maximum application rates and may include cumulative application rates for multiple applications of MCPA. Therefore, we cannot provide a table listing application techniques and rates only, because this would only apply to single applications. Providing buffer zones based on single application rates for each crop would make the buffer zone tables even more onerous and difficult to follow.

The goal of terrestrial buffer zones is to mitigate spray drift outside of the target spray area and protect non-target terrestrial habitat. When MCPA is applied to a registered use site, the adjacent areas such as meadows, grasslands, woodlots and shrublands, if not previously treated, are considered non-target areas and must be protected by buffer zones. These previously untreated non-target areas are considered sensitive terrestrial areas. As indicated above, grasslands or meadows require buffer zones. Sites managed as cropland such as pastures, haylands and rangeland do not require buffer zones for protection of terrestrial habitats. The PMRA will provide more guidance on “sensitive” habitats following the results of a workshop to examine the definition of “habitat” and the protection goals for these habitats.

A buffer zone strategy document was completed and is available on the PMRA website as Regulatory Proposal PRO2005-06, *Agricultural Buffer Zone Strategy Proposal*. It provides options for users on how to reduce buffer zones for agricultural applications. Buffer zones for aerial uses are risk-based and calculated using the AgDisp v. 8.15 model with toxicological input provided by the MCPA Task Force III. They are only applicable to non-target areas downwind of spray drift. Areas upwind of spray applications do not require buffer zones.

4.17 Comment
The buffer zones proposed in PRVD2007-01 would prevent users from completing their weed management programs without significant economic loss. Although the risk assessment for ecological effects uses a highly sophisticated spray drift model, the hazard endpoints (the other half of the risk equation) are extreme worst-case values. A number of assumptions used in the buffer zone modelling process include application rate, release/boom height, wind speed, nozzle classification, droplet size, water volume and toxic endpoint. Most of these do not significantly affect the buffer zone distance. However, there may be opportunities for the PMRA to reconsider the assumption made for some of these that do have more significant impact for aerial application.

Response
The model inputs mentioned do in fact have significant bearing on the estimation of the buffer zone distances. For parameters such as droplet size, water volume and application rate, these are the inputs obtained from the MCPA product labels and as such are "assumed" to be those observed by applicators. The PMRA realizes that other factors come into play other than the parameters considered in the modelling of buffer zones. It should be noted, however, that the PMRA requires sound scientific data before any assumptions that mitigate habitat exposure are considered.

4.18 Comment
In the case of terrestrial habitat toxic endpoints, the most sensitive species chosen was worst case and very conservative given the long period of use of this product without significant issues. The choice of lettuce, radish and tomato (effect concentration 25% [EC_{25}] = 0.01 kg a.e./ha) as the most sensitive indicator species does not reflect a plant-community-based endpoint, an approach that could significantly refine the terrestrial risk assessment.

Response
The PMRA recognizes the difficulty of extrapolating from a single species endpoint to a community endpoint. Thus, it will consider proposed risk assessment methods/approaches that would address this uncertainty as well as methods for the determination of a community-based endpoint. It also should be noted that the PMRA has historically requested from registrants plant data that are more appropriate for the risk assessment of terrestrial habitats.

4.19 Comment
Buffer zones are not required when spraying rights-of-way nor should they be required when applying a pest control product adjacent to an area that is an approved use site or contains a predominate species or plant family which is not affected by the active ingredient. For example, a buffer zone should not be required when applying MCPA to a field of wheat adjacent to a grassland or meadow where the predominate species is grass. Similarly, application to wheat adjacent to a rangeland or pasture should not require a buffer zone. In addition, if sensitive habitat are to be listed on labels, the label should reflect product-specific phraseology rather than generic statements that list all sensitive habitat; otherwise the user is unclear as to what needs protecting. For MCPA, grasslands and meadows need not be listed as sensitive habitat since they are managed sites and MCPA is either registered on these use sites or these use sites contain predominantly grass species upon which MCPA has no effect. A simple label statement that helps alleviate some of the uncertainties around this issue would be:

> Buffer zones are not required when spraying rights-of-way or areas adjacent to other labelled use sites or areas where the predominant species are grasses.

In addition, the PMRA needs to communicate that it is not its intent to require buffer zones for temporary water bodies (e.g. sloughs, ponds, prairie potholes). It is suggested that a clarification statement is needed such as:

> Temporary water bodies that collect spring runoff but do not provide permanent habitat do not require protection with buffer zones.

Response
Meadows, rangelands and pastures are terrestrial (vegetated) areas that do not require buffer zones for their protection. However, with the application of MCPA to meadows, rangelands and pastures, buffer zones are required to protect non-target vegetated areas other than meadows, etc., as well as aquatic habitats. When MCPA is applied to a wheat field, the adjacent grassland is considered a non-target area and must be protected by buffer zones since it may contain other non-grass species that are considered sensitive terrestrial habitat.

The question of sensitive habitats will be addressed at a workshop scheduled for April 2008. The current definition of sensitive terrestrial habitat can be found in PRO2005-06.

Temporary bodies of water do not require buffer zones. Sloughs, ponds and potholes are not temporary water bodies. The definition of temporary water body can be found in PRO2005-06. It is defined as follows:

> ...an area covered by water only some of the time and the water holding period is not regular or seasonal. An example of this kind of water body is the lower part of a field flooded after a heavy rain or runoff.

Seasonal water bodies do need to be buffered if there is water in them during application. A seasonal water body is defined as follows:

> ...an area covered with water only part of the year **and** for which flooding occurs in subsequent years on a regular basis. This will depend on climatic conditions and patterns. An example of this kind of water body is an aquatic area with water in the spring and summer but that dries out in the fall and winter.

4.20 Comment
There is concern regarding the buffer zones that are being proposed when the user community has been excluded from discussions. It is understood that discussions have been occurring at the Federal, Provincial, Territorial Committee on Pest Management and Pesticides regarding appropriate buffer zones. However, creating buffer zones before the final regulatory directive has been established without broad-based consultation does not seem appropriate.

Response
The FPT Committee on Pest Management and Pesticides is not a stakeholder committee. Stakeholders do have their own grower groups and the publication of a consultation document (e.g. PRVD) is the method the PMRA uses to solicit stakeholder and public input during the re-evaluation process of a pesticide.

4.21 Comment
Buffer zones may severely limit the ability of farmers and ranchers to control invasive weeds and protect their crops. Typically, users want to ensure that the perimeters of a field or pasture are sprayed to prevent the encroachment and spread of invasive species. This has the desired outcome of reducing the amount of pesticide required to control the invasive plants. The proposed buffer zones will have the opposite effect by leaving outside edges untreated and

susceptible while at the same time increasing the amount of pesticide required to protect the managed area.

Response
The PMRA did approach the provinces regarding coordinating the implementation of buffer zones with provincial noxious weed regulations. However, the issue is unresolved. The issue of invasive weeds will be addressed at a future workshop being planned by the PMRA on defining terrestrial habitats.

4.22 Comment
Clarification is requested as to the reasoning behind the PMRA suggesting a buffer zone in PACR2007-06 for 2,4-D and recommending no buffer zone in the PRVD for MCPA (PRVD2007-01), which reads as follows:

> When MCPA is used in agricultural crops, any adjacent rangelands and pastures do not require buffer zones.

Response
This statement for MCPA is also applicable to 2,4-D.

4.23 Comment
The "solubility of water" is actually the solubility of the MCPA ion in buffered solutions. The solubility of MCPA in unbuffered water is 0.395 g/L. The saturated solution is pH 1 as reported in Hopkins (1987).

Response
The information on the solubility in water was that of MCPA acid when it was added to buffered water at pH 5 to 9. The derivatives, MCPA-DMA and MCPA-Na^+, are more soluble than the acid at environmental pH (pH 5–9). The derivative, MCPA-2-EHE, is sparingly soluble in water at pH 5. The solubility of MCPA at pH 1 is 0.39 g/L.

4.24 Comment
The following statement should also reflect that MCPA DMA and MCPA Na^+/K^+ dissociate into ionic materials and not into MCPA:

> "Unlike MCPA DMA and MCPA Na^+/K^+, MCPA (acid) is not "very soluble in water ...."

Such a designation is normally used to indicate undissociated MCPA acid.

Response
It is understood that an acid (such as MCPA) exists as an ion in aqueous solution. As a H^+ ion donator, MCPA can be represented as $MCPA^-$. However, by convention, this is not a common designation as it is known that acids exist in the ionic form in aqueous solution.

4.25 Comment

A more recent study (Harwood 2001) was submitted to the PMRA in 2003 that demonstrates the acute and contact LD_{50} for bees is greater than 200 µg/bee.

Response

The PMRA will not consider a higher LD_{50} value unless a scientific rationale is presented to indicate otherwise. The PMRA considers the most sensitive endpoint in the risk assessment. Regardless, the PMRA reported the acute contact LD_{50}s for MCPA to be greater than 100 µg/bee, indicating it was relatively non-toxic to bees (according to the classification scheme of Atkins et al. 1981). Similarly, MCPA-Na^+ salt was relatively non-toxic as the acute oral LD_{50} was 94.4 µg a.e./bee, which is equivalent to an application rate of 105 kg a.e./ha. With MCPA-DMA, the acute contact no observed effect level (NOEL) was reported to be 13 µg a.e./bee and is equivalent to an application rate of 14.6 kg a.e./ha.

4.26 Comment

The acute oral toxicity studies used gavage dosing and are of questionable significance. Birds will normally only be exposed to MCPA following application of spray dilution, in which case it will form part of the diet. The dietary exposure levels are therefore relevant for the assessment of environmental effects.

Response

Acute oral toxicity studies are more reflective of dose-related effects, unlike dietary studies where there could be considerable uncertainty with the actual dose received through the diet. The risk assessment on birds is based on the contamination of the diet for both the acute oral and dietary endpoints.

4.27 Comment

There were several tests on *Lemna gibba.* The NOEC and EC_{50} from the tests quoted are outliers and reflect a set of conditions that have not been reproduced. The MCPA Task Force III will submit additional evidence to indicate that toxicity to *Lemna* is orders of magnitude higher than the stated value.

Response

The reported EC_{50}s for *Lemna gibba* by the MCPA Task Force III are 170, >2462, 2600, 200, 124, 87 and 1520 µg/L. The PMRA recently reassessed the *Lemna* endpoint as part of the updated risk assessment. An EC_{50} value of 124 µg/L (cited by the MCPA Task Force III, above) was considered by the PMRA together with a safety factor of 2 to attain an assessment value of 62 µg/L. It should be noted that the PMRA routinely considers the most sensitive endpoint in the assessment of risk. In addition, the study reviewed by the PMRA from which the EC_{50} of 124 µg/L was derived was deemed acceptable. Furthermore, the MCPA Task Force III did not submit the raw data for the other studies from which the other cited endpoints (other than EC_{50} = 124 µg/L) were derived.

5.0 Comments with Respect to Value

5.1 Comment

The details of the product listings for MCPA were current as of 13 July 2005 in the consultation document. It is recommended that, if such product listings are to be included in the final Re-evaluation Decision document, an up-to-date (i.e. less than six months prior to publication) tabulation of registration details be captured.

Response

The risk assessments presented in this PRVD document were based on the uses as listed in the document, which were registered when the re-evaluation process of this active started and were therefore considered current at that time. Note that while a number of products were discontinued during the re-evaluation period, the use profile of MCPA remained static.

5.2 Comment

The industry is already implementing two application treatments per year (plus spot treatments) with this herbicide. Can it be recommended that application frequency be reduced?

Response

Mitigation measures are usually proposed when risk assessments warrant such action. MCPA risk assessments did not trigger a proposal to mitigate risks through reduction of application frequency nor did the MCPA Task Force III or the registrants indicate a wish to decrease the number of applications. Thus, reduction of application frequency will not be recommended.

Appendix II Label Changes Required for Increased Protection to Human Health and the Environment

In addition to the statements already on the label, the following label statements must be added to the existing text.

1.0 Expression of the Guarantee—All Products

The guarantee statement on the labels of all products must be revised to specify the form of MCPA contained (i.e. one of the forms indicated in PRVD2007-01, Table 2.4.1) and the proportion of MCPA acid equivalents. For example, for the 2-EHE form, the guarantee should read “MCPA, present as the 2-ethylhexyl ester... y% a.e.” for solid products, or “y g a.e. / L” for liquid products, where “y” is the equivalent concentration of MCPA as the acid.

2.0 Human Toxicology Statements

Labels of technical, manufacturing concentrate and commercial class products containing MCPA must include the following.

> **TOXICOLOGICAL INFORMATION**
> High concentrations of MCPA may cause severe irritation to the eyes.*
> Symptoms of overexposure to MCPA could include slurred speech, twitching, jerking and spasms, drooling, low blood pressure and unconsciousness. Treat symptomatically.
>
> * *The statement concerning eye irritation may be modified by product-specific data.*

3.0 Personal Protective Equipment and Restricted-Entry Intervals Relating to Occupational Exposure

For asparagus, barley, rye, wheat, oats, canary grass/seed, cereals (fall-sown), cereals underseeded with legumes, corn (field and sweet), flax, grass (established hay and forage, grass for seed, pastures and rangeland, grass seedlings), legumes (established alfalfa, clover [alsike and red], seedling alfalfa, birdsfoot trefoil and clover), peas (field, canning, processing), stubble, summer fallow and spruce seedlings for reforestation (groundboom application), the following label statements are required.

- Mixers, loaders and applicators must wear a long-sleeved shirt, long pants, socks, shoes and chemical-resistant gloves. Aerial applicators and applicators using a closed cab are not required to wear chemical-resistant gloves.

- Re-entry is not permitted until 12 hours after application for all agricultural scenarios.

- For hand harvesting of corn (field and sweet), re-entry is not permitted until 15 days after application. As such, a preharvest interval (PHI) of 15 days after application is required.

- For asparagus, grasses grown for seed, summer fallow and stubble land, a maximum of 2 applications is permitted per season with a minimum retreatment interval of 21 days.

- For established grasses, grass seedlings, pastures and rangeland, and established legumes, a maximum of 2 applications is permitted per season, with a minimum retreatment interval of 90 days.

For spot treatment or broadcast treatment of non-cropland/industrial sites listed in Section 2.3 (PRVD2007-01), the following statements are required.

- Applicators must wear a long-sleeved shirt, long pants and chemical-resistant gloves (except for aerial applicators during application).
- For spot treatment of all industrial sites using high-pressure handwands, do not exceed 900 litres of "ready to use"solution (equivalent to 9 kg a.i.) per day per individual applicator. For application using handheld equipment, use a maximum concentration of 0.01 kg a.e./L. For broadcast treatment of industrial sites, a maximum of 2 applications are permitted per season, with a minimum retreatment interval of 21 days.

For products applied by air, the following statements are required:

- Aerial applicators must wear long pants and a long-sleeved shirt.
- Mixers/loaders must wear long pants, a long-sleeved shirt and chemical-resistant gloves during mixing, loading, clean-up and repair activities.
- Aircraft must be closed cab.
- Mixer/loader and applicator must be different individuals.
- No human flaggers permitted.

For all products that do not include use on residential turf, the following statement must appear on the product label:

> Do not use in residential areas, which are defined as sites where bystanders may be present during or after spraying , including homes, schools, parks, playgrounds, playing fields and public buildings.

For products to be used on sod farms and spruce seedlings, a restricted-entry interval (REI) of 1 day is required.

Establish a maximum use rate of 1.7 kg a.e./ha for residential and recreational areas.

4.0 Statements Reducing Dietary Exposure

When used on barley, oats, rye, wheat, field corn, peas, legumes, stubble land, pastures, rangelands, roadsides, uncropped land:

- 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.

5.0 Statements Reducing Environmental Exposure

In addition to buffer zones, the following precautionary measures must appear on product labels.

The following label statement must be included under **ENVIRONMENTAL HAZARDS**:

> Toxic to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE.

The following label statement must be included under **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) coarse 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) coarse classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length MUST NOT exceed 65% of the wingspan or rotorspan.
>
> For application to rights-of-way, buffer zones for protection of sensitive terrestrial habitats are not required; however, the best available application strategies which minimize off-site drift, including meteorological conditions (e.g. wind direction, low wind speed) and spray equipment (e.g. coarse droplet sizes, minimizing height above canopy), should be used. Applicators must, however, observe the specified buffer zones for protection of sensitive aquatic habitats.

Surface runoff

To reduce runoff from treated areas into aquatic habitats, consider the characteristics and conditions of the site before treatment. Site characteristics and conditions that may lead to runoff include, but are not limited to, heavy rainfall, moderate to steep slope, bare soil, poorly draining soil (e.g. soils that are compacted, fine-textured, or low in organic matter such as clay).

Avoid applying this product when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip (buffer zone) 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. sand, loamy sand and sandy loam soils) and/or the depth to the water table is shallow.

Buffer Zones to Protect Sensitive Habitat

Use of the following spray methods or equipment DO NOT require a buffer zone: handheld 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.

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture.

Method of Application	Crop		Buffer Zones (metres) Required for the Protection of:				
			Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:		Terrestrial Habitat
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m	
Field sprayer*	Cereals, flax, grasses, turf, corn, canaryseed, legumes, stubble, summer fallow, non-cropland, vegetable crops, rights-of-way,** industrial sites, forestry (spruce seedlings)***		1	1	1	1	4
Aerial	Terrestrial Food and Feed Crops						
	Asparagus	Fixed	5	1	1	1	85
		Rotary wing	5	1	1	1	70
	Cereals, corn, flax	Fixed wing	1	0	1	0	60
		Rotary wing	1	0	1	0	50
	Grasses	Fixed wing	1	0	1	1	75
		Rotary wing	1	0	1	1	60
	Legumes, peas	Fixed wing	1	0	0	0	25
		Rotary wing	1	0	0	0	25
	Pastures, rangeland, stubble, summer fallow	Fixed wing	5	1	1	1	100
		Rotary wing	4	1	1	1	80
	Non-Crop Uses:						
	Non-cropland, including rights-of-way,** industrial sites	Fixed wing	30	1	20	1	200
		Rotary wing	20	1	10	1	100

*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%.
**Buffer zones for the protection of terrestrial habitats are not required for use on rights-of-way, including railroad ballast, rail and hydro rights-of-way, utility easements, roads, and training grounds and firing ranges on military bases.
***Buffer zones for protection of terrestrial habitats are not required for application to preparation sites for spruce seedlings.

6.0 Description of Registered Use Sites

If used on the label, the terms “non-cropland” and “industrial sites” must be defined specifically and indicated clearly on the label (e.g. for use on rights-of-way for transportation, rights-of-way for utility lines, and in airports, wastelands, industrial parks, etc.).

The designation “Canary Grass” or “Annual Canary Grass” must be revised on the label as “Canary Seed (*Phalaris canariensis*)”.

7.0 Changes to Maximum Application Rates, Maximum Number of Applications per Year

Note that changes are not required for sites that are not listed in the table below.

Site	Maximum Rate for a Single Application (g a.e. of MCPA/ha)	Cumulative Maximum Rate per Season (g a.e. of MCPA/ha)	Maximum Number of Applications per Year
Use-site Category 30: Turf			
Fine turf	1700	—	2
Use-site Category 13: Terrestrial Feed Crops			
Legumes (seedlings)	300	300	1
Grasses, established (hay and forage)	1120	2240	2
Pasture/Rangeland	1750	3500	2
Use-site Categories 13 and 14: Terrestrial Feed Crops and Terrestrial Food Crops			
Barley	875	875	1
Oats	875	875	1
Rye	875	875	1
Wheat	875	875	1
Corn (field)	850	850	1
Use-site Categories 7, 13 and 14: Industrial Oilseed Crops and Fibre Crops, Terrestrial Feed Crops and Terrestrial Food Crops			
Flax	875	875	1
Use-site Category 16: Industrial and Domestic Vegetation Control Non-Food Sites			
Non-cropland areas—broadcast treatment	1680	3360	2
Non-cropland areas—spot treatment	3360	—	—