Health Canada
Pest Management Regulatory Agency

Santé Canada
Agence de réglementation de la lutte antiparasitaire

Re-evaluation Note

REV2007-11

Preliminary Risk and Value Assessments of Methamidophos

The purpose of this document is to inform registrants, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has completed preliminary risk and value assessments of methamidophos. This re-evaluation note provides a summary of these preliminary assessments based on the data and information reviewed. The preliminary assessments identified potential risks to the environment, to workers both during application and during re-entry activities as well as to the general population through drinking water exposure. The PMRA is requesting further data/information to finalize the preliminary risk and value assessments and to propose regulatory action.

The PMRA will accept written comments and information up to 60 days from the date of publication of this document. All comments should be forwarded to Publications at the address below.

The PMRA will review the information received, revise the risk and value assessments as necessary and propose regulatory action in a future Proposed Re-evaluation Decision document.

(publié aussi en français)

4 September 2007

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

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6605C
Ottawa, Ontario
K1A 0K9

Internet: pmra_publications@hc-sc.gc.ca
www.pmra-arla.gc.ca
Information Service:
1-800-267-6315 or 613-736-3799
Facsimile: 613-736-3758

Canada

ISBN: 978-0-662-46712-0 (978-0-662-46713-7)
Catalogue number: H113-5/2007-11E (H113-5/2007-11E-PDF)

Foreword

Health Canada's PMRA has completed preliminary risk and value assessments for the active ingredient methamidophos and its label uses on a wide variety of food and industrial oilseed crops. The registrants of the technical grade active ingredient are Bayer CropScience Inc. and Arysta Lifescience Corp.

The preliminary assessments presented in this document identified potential risks to the environment, to workers both during application and during re-entry activities as well as to the general population through drinking water exposure. At this time, these assessments support a phase out from the Canadian market of methamidophos and all associated uses, i.e. on broccoli, Brussels sprouts, cabbage, cauliflower, head lettuce, potato and canola. Based on information available to the PMRA, there is little reported use of products containing methamidophos in Canada, and viable alternatives are registered for these uses.

The PMRA is soliciting from the public and all interested parties information that may be used to refine the occupational, dietary (water) and environmental assessments and/or mitigate risks. Further information is also requested on the value of methamidophos. The PMRA will review the information received, revise the assessments as necessary and propose regulatory action in a future Proposed Re-evaluation Decision document.

Table of Contents

1.0 Purpose

This document describes the PMRA's preliminary risk and value assessments of the insecticide methamidophos and its registered uses. It includes assessments of risk to human health and the environment as well as information on the value of methamidophos to pest management in Canada. By way of this document, the PMRA is soliciting comments and input to the risk and value assessments of methamidophos from interested parties. Such comments and input could include additional data or information to further refine the risk assessment, such as typical use-pattern information, information concerning percentage of crop treated, area treated per day or could address the PMRA's risk assessment approaches and assumptions as applied to methamidophos. Further information regarding the effectiveness and extent of use of the alternatives to methamidophos could be used to refine the value assessment.

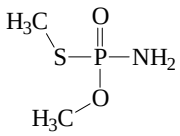
2.0 Re-evaluation of Methamidophos

Methamidophos is one of the pesticides subject to re-evaluation in Canada as announced in Re-evaluation Document REV99-01, *Re-evaluation of Organophosphate Pesticides*. Methamidophos is a broad spectrum, Resistance Management Group 1B (organophosphate) insecticide which inhibits the enzyme acetylcholinesterase, interrupting the transmission of nerve impulses. It works by contact and ingestion and has a systemic action. Methamidophos is a breakdown product of acephate, a closely related organophosphate pesticide.

2.1 Identity of the Active Substance

Active substance	Methamidophos
Function	Insecticide
Chemical name	
International Union of Pure and Applied Chemistry (IUPAC)	O,S-dimethyl phosphoramidothioate
Chemical Abstracts Service (CAS)	O,S-dimethyl phosphoramidothioate
Chemical family	Organophosphate
CAS Registry Number	10265-92-6
Molecular formula	$C_2H_8NO_2PS$
Molecular weight	141.13

Structural formula



2.1.1 Identity of Relevant Impurities of Toxicological, Environmental and/or Other Significance

Based on the manufacturing process, composition of raw materials and the chemical structure of methamodophos, the technical grade active ingredient is not expected to contain impurities of toxicological concern.

2.2 Description of Registered Methamidophos Uses

Methamidophos is registered for use on industrial oilseed crops as well as terrestrial feed and food crops.

Appendices I and II list methamidophos products registered in Canada and details of their uses. All registered uses of methamidophos are supported by the registrants and were considered in the health and environmental risk assessments.

3.0 Effects Having Relevance to Human Health

3.1 Toxicology Summary

The toxicology database supporting methamidophos is primarily based on studies available from the registrant. In acute toxicity studies, methamidophos was highly toxic via the oral route of exposure in rats and mice, via the dermal route in rabbits and via the inhalation route in rats. It was moderately irritating to eyes and slightly irritating to skin; several treated animals died shortly after dermal or ocular application. These findings suggest that methamidophos is rapidly absorbed via these routes. It was not found to be a skin sensitizer. Acute toxicity signs induced by methamidophos via all routes are consistent with signs of cholinesterase intoxication and include tremors, salivation, ataxia, depression, bloody tears, lacrimation, decreased motor activity, loss of coordination, laboured breathing and death. With oral exposure, methamidophos was readily absorbed and rapidly eliminated with little tissue retention. Excretion occurred via the urine and expired air as well as, to a lesser degree, in the faeces. The identified urinary metabolites were unchanged methamidophos, O,S-dimethyl phosphorothioate, methyl dihydrogen phosphate and phosphoric acid.

Following single and repeated dosing, the most sensitive indicator of toxicity was the inhibition of acetylcholinesterase, an enzyme necessary for the proper functioning of the nervous system. Acetylcholinesterase was affected by oral, dermal and inhalation routes with no appreciable species or gender differences. Duration of oral exposure had little effect on toxicity in rats (subchronic to chronic, 8-week, 13-week, and 2-year dietary exposure) based on no observed adverse effect levels / lowest observed adverse effect levels (NOAELs/LOAELs); however, an increasing duration of inhalation exposure did result in greater toxicity. Cholinergic signs of

toxicity, reduced body-weight gain and food consumption (mice, rats and rabbits) were also observed at higher doses. Methamidophos showed no evidence of tumourigenicity in either rats or mice following chronic dosing. While most genotoxicity studies showed no significant response, positive results were obtained in an in vitro cytogenic assay at very high or cytotoxic doses. In addition, published literature suggested positive cytogenetic effects in mouse bone marrow and spleen cells in in vivo and in vitro assays specific to the Swiss strain. These findings were not replicated in several in vivo bone marrow cell assays in CD-1 mice.

In acute and subchronic oral neurotoxicity studies in rats, no treatment-related neuropathy was evident although cholinergic signs of toxicity were demonstrated. No histopathological findings of neuropathy in rodents were evident in the remainder of the database. However, in hen studies, methamidophos (racemate and enantiomers) produced signs of delayed neurotoxicity at high doses (greater than 10-fold the oral lethal dose to 50% [LD_{50}] values) under antidotal protection. The signs included abnormal gait, ataxia, motor incoordination and paralysis several days (i.e. day 18) after a single oral exposure. Inhibition of neuropathy target esterases (NTE) in the brain and spinal cord (sciatic nerve occasionally reported) was reported in delayed neurotoxicity studies in the hen, but no neuropathy was evident in the studies in which pathology was undertaken. NTE reactivation studies indicated that most of the depressed brain NTE by the racemate or the D(+)-isomer of methamidophos could be reactivated in vitro, indicating that the enzyme had not been modified. On the contrary, the depressed brain NTE by the L(-)-isomer of methamidophos was not reactivated in vitro to any significant extent. Similar results were demonstrated in the spontaneous in vivo reactivation of the D(+) and L(-)-isomers. These findings suggest that methamidophos (especially with a high content of the L(-)-isomer) has delayed neurotoxic potential at very high doses. Similarly, information in the open literature indicates that methamidophos could cause delayed neurotoxicity in humans following exposure to excessive, life threatening concentrations.

The developmental toxicity studies in rats and rabbits showed no evidence of teratogenic effects and no additional sensitivity of the fetus following in utero exposure to methamidophos. Developmental effects in rats (decreased fetal weight and increased fetal skeletal variations) were observed only in the presence of maternal toxicity. In the two-generation reproductive toxicity study in rats, no sensitivity of the young was demonstrated at the levels tested. Parental and offspring effects included depressed cholinesterase activity and decreased weight gain. Pup viability was also affected. Reproductive effects included increased stillbirths and, in the supplemental study, decreased litter size and fertility (decreased sperm-positive F_0 and F_1 dams giving birth) at dose levels equal to or higher than those causing cholinesterase inhibition. Published literature suggests that methamidophos might have the potential to produce transmissible adverse embryonic effects following an acute intraperitoneal paternal exposure; however, limitations of the data with respect to route and animal numbers suggest a need for further investigation.

Reference doses have been set based on NOAELs for the most sensitive indicator of toxicity, namely acetylcholinesterase inhibition. These reference doses incorporate various uncertainty factors to account for extrapolating between laboratory animals and humans and for variability within the human population. An additional safety factor has been used to provide an additional safeguard for the delayed neurotoxic potential of methamidophos. As this potential has been

demonstrated in hens and in humans, it is considered prudent to include this safety factor when using rodent studies for risk assessment given that rodents are generally a less sensitive model for detecting delayed neurotoxicity.

Under the new *Pest Control Products Act*, an additional 10-fold factor is required to protect children and pregnant females from relevant endpoints of concern or any database uncertainty regarding a potential for increased sensitivity in these population subgroups. A different factor may be determined to be appropriate on the basis of reliable scientific data. In the case of methamidophos, the 10-fold *Pest Control Products Act* factor has been reduced to 1-fold because additional safety factors have already accounted for database concerns (i.e. delayed neurotoxic potential).

A developmental neurotoxicity study has been submitted by the technical registrant. The review of this study will be completed and reported in a future Proposed Re-evaluation Decision document.

The toxicology endpoints used in the risk assessment of methamidophos are summarized in Appendix IV.

3.2 Occupational and Residential Risk Assessment

Occupational and residential risks are estimated by comparing potential exposures with the most relevant endpoints from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean exposure will result in adverse effects. However, mitigation measures will be necessary to reduce exposure.

For the short- or intermediate-term dermal risk assessment, the NOAEL of 0.75 mg/kg bw/day from the rat 3-week dermal toxicity study is selected. This NOAEL is based on depressed cholinesterase (brain cholinesterase [BChE], erythrocyte cholinesterase [EChE] and plasma cholinesterase [PChE]) observed at the next higher dose of 11.2 mg/kg bw/day. The available toxicology database suggests that increased duration of oral exposure (subchronic–chronic) would not significantly increase toxicity of methamidophos. This study is selected because the route and duration of exposure are considered appropriate and the endpoint affected (depressed cholinesterase) is consistent with the remainder of the database. A target MOE of 300 is required; this accounts for interspecies extrapolation (10-fold) and intraspecies variability (10-fold) and includes an additional safety factor of 3-fold to account for the delayed neurotoxic potential of methamidophos.

For the short-term inhalation risk assessment, the NOAEL of 0.0026 mg/L (equal to 0.53 mg/kg bw/day) from a 3-week inhalation toxicity study in rats is selected. This NOAEL is based on the cholinesterase inhibition (BChE, EChE and PChE) observed at the next higher dose level (0.012 mg/L) and above. This study is selected as the route and duration of exposure are considered appropriate and the endpoint affected is consistent with the remainder of the database. A target MOE of 300 is required to account for interspecies extrapolation (10-fold) and

intraspecies variability (10-fold) and includes an additional safety factor of 3-fold to account for the delayed neurotoxic potential of methamidophos.

For the intermediate-term inhalation risk assessment, the NOAEL of 0.001 mg/L (equal to 0.27 mg/kg bw/day) from a 13-week inhalation toxicity study in rats is selected. This NOAEL is based on the cholinesterase inhibition (BChE, EChE and PChE) observed at the next higher dose level (0.005 mg/L) and above. A target MOE of 300 is required to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold) and includes an additional safety factor of 3-fold to account for the delayed neurotoxic potential of methamidophos.

3.2.1 Occupational Mixer/Loader/Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders, applicators or other handlers. The major scenarios identified were the following:

- mixing/loading emulsifiable concentrate for aerial application to canola
- applying emulsifiable concentrate to canola using aerial application
- mixing/loading/applying emulsifiable concentrate using groundboom to terrestrial field crops.

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

Baseline PPE: long sleeved shirt and long pants
Minimum PPE: baseline PPE, cotton coveralls, gloves and respirator
Maximum PPE: baseline PPE, chemical-resistant coveralls, gloves and respirator
Engineering Controls: baseline PPE, closed packaging and gloves for mixing/loading; baseline PPE and closed tractor cab for application

No chemical-specific handler exposure data were submitted for methamidophos; therefore, daily dermal and inhalation exposure was estimated for the various application methods using the Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1). The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE. Exposure (mg/kg bw/day) is calculated as the product of the PHED unit exposure for a given scenario, the label application rate(s) and the area treated per day for a specific crop divided by body weight.

In most cases, the PHED did not contain appropriate data sets to estimate exposure to workers wearing cotton coveralls, chemical-resistant coveralls or a respirator. This was estimated by incorporating a 75% clothing protection factor for cotton coveralls, 90% protection factor for chemical-resistant coveralls and a 90% protection factor for a respirator into the unit exposure data.

Mixer, loader and applicator exposure estimates are based on the best available data at this time. The assessment might be refined with exposure data more representative of modern spray equipment and engineering controls.

Based on the methamidophos use pattern, mixer/loader/applicator exposure scenarios were considered to be short- to intermediate-term (< 6 months) in duration.

Occupational risk is estimated by comparing a calculated MOE to a target MOE incorporating safety factors protective of the most sensitive subpopulation. For methamidophos, the adverse toxicological endpoint of concern is the same regardless of exposure route; thus, it is appropriate to combine the MOEs into a single risk estimate. Combined MOEs greater than or equal to the target MOE of 300 do not require risk mitigation. Dermal and inhalation MOEs for mixing, loading and applying methamidophos are summarized in Appendix V.

In summary, all scenarios have calculated MOEs that are significantly below target MOEs even with maximum PPE or engineering controls.

3.2.2 Occupational Postapplication Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers who re-enter treated sites to conduct agronomic activities involving foliar contact (e.g. pruning, thinning, harvesting or scouting). Based on the methamidophos use pattern, there is potential for short- to intermediate-term (< 6 months) postapplication exposure by the dermal and inhalation routes. However inhalation exposure is considered to be negligible in outdoor postapplication scenarios because of the low vapour pressure of methamidophos and because the empirical data have generally shown postapplication inhalation exposures to be negligible.

Potential dermal exposure to re-entry workers was estimated using activity specific transfer coefficients (TCs) and dislodgeable foliar residue (DFR) studies. The TC is a measure of the relationship between exposure and DFRs for individuals engaged in a specific activity, and is calculated from the data generated in field exposure studies.

Postapplication risk is managed by establishing a restricted-entry interval (REI) for specific tasks. Pesticide residues dissipate and/or breakdown over time. An REI is the length of time required for the dislodgeable pesticide residues to dissipate to such a level that entry into a treated area does not result in unacceptable exposure.

Based on current label REIs and use pattern, potential postapplication exposure for re-entry workers performing any activity results in calculated MOEs that do not meet the target MOE of 300. Based on the currently available data, most REIs would need to be significantly increased in length to achieve the target MOEs. Calculated REIs for selected re-entry activities and a target MOE of 300 are shown in Appendix VI, Table 1. Most of these REIs are not practical for growers.

3.2.3 Residential Exposure and Risk Assessment

There are no registered residential uses of methamidophos. Residential exposure to methamidophos may occur as a result of the use of acephate in residential settings because acephate degrades to methamidophos. Residential methamidophos exposure resulting from the use of acephate was already addressed during the re-evaluation of acephate. It does not result in unacceptable risk to homeowners or children entering treated areas (See PACR2004-40, *Re-evaluation of Acephate*, dated 22 October 2004).

3.3 Dietary Exposure and Risk Assessment

Residues of methamidophos on food can occur following the use of acephate, which is also registered as a pest control product for use on food crops. To fully assess the potential dietary exposure, residues of methamidophos arising from both the use of acephate and methamidophos were considered in the dietary exposure and 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. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life. For example, 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, a pesticide with low toxicity may pose a risk if the exposure is high.

Acute and chronic dietary exposure and risk estimates were generated using the Dietary Exposure Evaluation Model (DEEM®) software and consumption data from the United Sates Department of Agriculture's Continuing Surveys of Food Intake of Individuals for 1994–1998.

3.3.1 Acute Dietary Exposure and Risk Assessment

Acute dietary risk is calculated considering food consumption and residue values in food. A probabilistic statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of methamidophos residue that might be eaten in a day. A value representing the high end (99.9^{th} percentile) of this distribution is compared to the acute reference dose (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 from residues is less than the ARfD, the expected intake is not considered to be of concern.

To estimate acute dietary risk (1 day), the NOAEL of 0.3 mg/kg bw from the acute neurotoxicity study in rats is selected for risk assessment. This NOAEL is established based on depressed cholinesterase (BChE, EChE and PChE) at the next highest dose of 0.7 mg/kg bw. An overall safety factor of 300 is required to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold), and includes an additional safety factor of 3-fold to account for

the delayed neurotoxic potential of methamidophos. The ARfD was calculated to be 0.001 mg/kg bw (0.3 mg/kg bw ÷ 300). This value was considered to be protective of all populations including infants and children.

The acute dietary exposure was assessed in a mixed tier probabilistic assessment, using anticipated residue data from feeding studies, available monitoring data and the percentage of crop treated as refinements for commodities on which methamidophos is registered in the United States and in Canada. The acute potential daily intake accounted for < 75% (99.9^{th} percentile) of the ARfD for all subpopulations. Therefore, the acute dietary risk from methamidophos is not considered to be of concern.

3.3.2 Chronic Dietary Exposure and Risk Assessment

The chronic dietary risk is calculated by using the average consumption of different foods and the average residue values on those foods over a 70-year lifetime. This expected intake of residues is compared to the acceptable daily intake (ADI), which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the expected intake from residues is less than the ADI, the expected intake is not considered to be of concern.

To estimate dietary risk from the repeat or chronic exposure, the NOAEL of 0.03 mg/kg bw/day from the 8-week dietary toxicity study in rats is selected for risk assessment. The effect observed at this dose level was depressed brain cholinesterase at the next higher dose level (0.07 mg/kg bw/day). The available toxicology database suggests increased duration of oral exposure, i.e. subchronic to chronic, would not significantly increase toxicity of methamidophos. A 300-fold safety factor is required to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold), and an additional safety factor of 3-fold to account for the delayed neurotoxic potential of methamidophos. The ADI was calculated to be 0.0001 mg/kg bw/day (0.03 mg/kg bw/day ÷ 300). This value was considered to be protective of all populations including infants and children.

The chronic dietary exposure was assessed using anticipated residue data from feeding studies, available monitoring data and information on the percentage of crop treated as refinements for commodities on which methamidophos is registered in the United States and in Canada. The chronic potential daily intake accounted for < 55 % of the ADI for all population subgroups. Therefore, the chronic dietary risk from methamidophos is not considered to be of concern.

3.3.3 Drinking Water Exposure

Drinking water exposure was addressed by calculating drinking water levels of comparison (DWLOC). These can only be calculated if all other exposure scenarios (e.g. dietary or residential) are not of concern to the Agency. DWLOCs are based on the difference between the appropriate toxicology endpoints and the non-drinking water exposure and can be directly compared to estimated concentrations in drinking water.

The potential exposure from drinking surface water and ground water in muck soils exceeds the target level of acceptability. The acute DWLOC values ranged from 3.7 µg/L for children 1–6 years of age to 16 µg/L for the general population. The chronic DWLOCs ranged from 0.5 µg/L for infants to 2.5 µg/L for the general population. Estimated environmental concentrations (EECs) for drinking water, based on screening level models, were 1.8 µg/L for groundwater from muck soils, 8.2×10^{-5} µg/L in mineral soils (acute and chronic) and 27.3 and 1.56 µg/L for acute and chronic concentrations in surface water (Section 4.3).

As the acute and chronic EECs exceed the respective DWLOCs for all surface water scenarios and for the chronic ground water scenario with muck soils, acute and chronic exposure to methamidophos through the diet (food and drinking water) is of concern.

3.4 Aggregate Exposure and 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, and from all known or plausible exposure routes (oral, dermal and inhalation).

3.4.1 Acute and Chronic Aggregate Assessment

The timeframe for non-dietary residential exposure to methamidophos is only expected to be short-term. Therefore, the acute and chronic aggregate assessment is encompassed by the dietary and drinking water assessment. As discussed in Section 3.3, the acute and chronic exposure from food and drinking water is of concern.

3.4.2 Short-Term Aggregate Assessment

The short-term aggregate risk assessment encompassed potential short-term exposure to methamidophos residues on ornamentals treated with acephate in residential areas, dietary and drinking water exposure.

Although there are no residential uses of methamidophos, exposure is possible upon entering residential areas that have been previously treated with acephate, as methamidophos is a potential transformation product of acephate. Exposures resulting from use of acephate on ornamental plants in residential areas were assumed to co-occur with background (chronic) dietary and drinking water exposure for adults and youth. As acephate has only commercial class registrations, co-occurrence with homeowner applicator exposure was not considered.

The relevant duration of exposure to assess toxicological endpoints for this assessment would be a short-term exposure. Inhibition of brain cholinesterase was a common toxic effect among all routes of exposure. For assessment of the oral route of exposure, the NOAEL of 0.03 mg/kg bw/day from the 8-week dietary toxicity study in rats is selected based on inhibition of brain cholinesterase at 0.06 mg/kg bw/day. To assess the dermal component, the NOAEL of 0.75 mg/kg bw/day from the 3-week dermal study in rats was selected (brain cholinesterase inhibition at 11 mg/kg bw/day). No inhalation exposure is expected. For the short-term aggregate assessment, standard uncertainty factors are applied (10-fold for interspecies extrapolation and

10-fold for intraspecies variability) as well as an additional safety factor of 3-fold to address the delayed neurotoxic potential for a target MOE of 300. This MOE is considered to be protective of all populations.

The short-term aggregate (food and residential) risk is expressed in the form of an aggregate risk index (ARI). An ARI of 1.0 or greater is not of concern to the PMRA. As with the acute and chronic aggregate assessment, drinking water exposure was assessed by calculating DWLOC and comparing these values to the expected environmental concentration (EEC).

The ARIs of 1.06 and 1.08 for the adult and youth populations, respectively, were above the target ARI of 1.0; therefore, the ARIs are not considered to be of concern. Aggregate DWLOCs calculated for the short-term aggregate risk assessment were 0.19 µg/L for adults and 0.14 µg/L for youth. As the corresponding surface drinking water estimate (1.56 µg/L; see Section 4.3) exceeds the DWLOCs, the short-term aggregate exposure to methamidophos (food, drinking water and residential) is of concern.

4.0 Environmental Assessment

To conduct the environmental risk assessment of methamidophos, the PMRA used a deterministic approach that characterizes the risk by quotient method. With the quotient method, a risk quotient (RQ) is calculated as the ratio of the estimated environmental concentration to the effects endpoint of concern. RQs less than one are considered as a low risk for non-target organisms, whereas, RQs greater than one indicate some degree of risk.

In the assessment, estimated environmental concentrations for aquatic and terrestrial ecosystems were based on various recommended application rates (0.528–1.104 kg a.i./ha) and one application/season. Toxicity endpoints (acute and/or chronic) were chosen for the most sensitive species and used as surrogates for the range of species that could be exposed following treatment with methamidophos.

4.1 Environmental Fate

Available data indicate that methamidophos is non-persistent in the environment. In soil, biotransformation is an important route in transformation of methamidophos (aerobic soil the half-life was 0.5 day). In water, hydrolysis half-life is 309, 27 and 3.2 days at pH 5, 7 and 9, respectively; biotransformation was a more important route of transformation with the half-life of 4–8 days. Methamidophos is stable to phototransformation in water.

Methamidophos is non-volatile from moist soil and water surface as indicated by Henry's law constant (1.6×10^{-11} atm·m^3·mole^{-1}). The *n*-organic–carbon partition coefficient (log K_{ow}) of −0.796 indicates very low potential for bioaccumulation. Under field conditions, methamidophos is expected to be very highly mobile in soil (organic-carbon partition coefficient [K_{oc}] = 0.88).

4.2 Environmental Toxicology

Laboratory studies demonstrated that methamidophos was acutely and chronically toxic to a wide variety of organisms, including birds, mammals and aquatic invertebrates.

Methamidophos is classified as highly toxic to honey bees (LD_{50} = 1.37 µg a.i./bee). A lethal concentration to 50% (LC_{50}) of 34 mg a.i./kg soil was determined for earthworms. Methamidophos is very highly toxic to freshwater invertebrates (effect concentration 50% [EC_{50}] = 0.026 mg a.i./L) and slightly toxic to fish (LC_{50} = 25–34 mg a.i./L). It is slightly to highly toxic to estuarine/marine organisms (LC_{50} = 1.05–36 mg a.i./L). Methamidophos is very highly toxic to birds (LD_{50} = 1.78–10 mg a.i./kg) on an acute basis and slightly to very highly toxic (LC_{50} = 42–1650 mg a.i./kg) on a dietary basis. It has chronic adverse effects at levels greater than 3 mg a.i./kg. Methamidophos is highly toxic to mammals on an acute basis (LD_{50} = 13–18 mg a.i./kg). Methamidophos has chronic adverse effects on mammals at levels greater than 10 mg a.i./kg.

4.3 Concentrations in Drinking Water

Residues of methamidophos in drinking water sources in Canada were estimated in a Level 1 assessment using the Leaching Estimation and Chemistry Model (LEACHM) and the Pesticide Root Zone Model / Exposure Analysis Modeling System (PRZM/EXAMS). LEACHM was used to estimate the residues in ground water, whereas the residues in dugouts and reservoirs were estimated using the PRZM/EXAMS. For residues in ground water, the concentration was estimated to be 1.8 µg a.i./L. For residues in reservoirs, the acute and chronic exposure concentrations were estimated to be 27.3 and 1.56 µg a.i./L, respectively. For dugouts, the acute and chronic exposure concentrations were estimated to be 20 and 1.2 µg a.i./L, respectively. In muck soil, the values for reservoir are 53.9 and 3 µg a.i./L for acute and chronic exposure, respectively. These concentrations represent the upper-bound exposure concentration.

For residues in ground water, the concentration was estimated to be 8.2×10^{-5} µg a.i./L for mineral soils and 1.8 µg a.i./L for muck soils. The PMRA notes there was no evidence of contamination in groundwater from American monitoring studies.

A search for Canadian methamidophos water monitoring data revealed that routine analysis for methamidophos is not conducted. The limited monitoring data in the United States combined with the lack of monitoring data within Canada did not allow for the residues of methamidophos in potential drinking water sources to be estimated using statistical analysis of monitoring data. Therefore, the drinking water values available for use in the exposure risk assessment at this time are those estimated by modelling.

4.4 Terrestrial Risk Assessment

The results of this screening assessment identified various levels of risk for non-target terrestrial organisms exposed to methamidophos.

Bees and other beneficial insects may be exposed to methamidophos through spray deposit. Based on the acute contact toxicity (LD_{50} = 1.5 kg a.i./ha), moderate acute risk to bees is anticipated from the use of methamidophos, when use involves application to crops in blossom (RQ = 3–7).

Birds could be exposed to methamidophos drift or by consumption of contaminated food (e.g. seeds, insects or grasses). Based on the acute oral toxicity of methamidophos to birds (LD_{50} = 1.78 mg a.i./kg; no observed effect level [NOEL] = 0.178 mg a.i./kg) and using the PMRA standard exposure scenarios, it was determined that birds would have to consume contaminated food sources for 0.008–0.02 day to reach LD_{50}. For no-observable effects on a population, birds can consume contaminated food for up to 0.0008–0.002 days (NOEL). As the number of feeding days required for adverse effect is less than one, there is an acute risk for birds consuming contaminated food sources. Assessment of dietary and reproduction toxicity to birds resulted in RQs of 22–46 and 30–64, respectively. Based on this scenario, chronic toxicity of methamidophos is classified as a high risk for birds.

Recently, there have been concerns regarding the toxicity of methamidophos through dermal exposure in birds at rates within the range currently registered.

Reported incidents in the United States and field studies indicate that there is high acute risk for birds. Data from field studies indicate that methamidophos residues were found in animals and their food items. Birds have been shown to have brain cholinesterase inhibition of 40–65%. Data from the literature suggest that the migratory patterns of adult birds that are exposed to acephate/methamidophos are adversely affected. Methamidophos may have induced aberrant migratory orientation and behaviour by affecting the memory of the adults regarding migratory routes and wintering grounds. Birds may veer off their migratory routes, become lost and die of exhaustion, which may effect population levels.

Wild mammals could be exposed to methamidophos by ingestion of contaminated food (e.g. grass, seeds and leafy plants). Based on the acute oral toxicity of methamidophos to small mammals (LD_{50} = 13 mg a.i./kg; NOEL = 1.3 mg a.i./kg) and using the standard PMRA exposure scenarios, it was determined that animals would have to consume contaminated food sources for 0.03–0.7 days to reach LD_{50}. For no-observable effects on population, animals can consume contaminated food for up to 0.09–0.19 days (NOEL). As the number of feeding days required for adverse effects is less than one, there is an acute risk for small mammals consuming contaminated food. Assessment of chronic (reproduction) toxicity to mammals resulted in RQs of 26–56. Based on this scenario, chronic toxicity of methamidophos is classified as high risk for small mammals.

4.5 Aquatic Risk Assessment

The results of this screening assessment identified various levels of risk for non-target aquatic organisms exposed to methamidophos.

Aquatic organisms can be exposed to methamidophos that enters aquatic systems through spray drift. For the laboratory-derived data, RQ values were based on estimates of the acute no observed effect concentration (NOEC) for the most sensitive species (i.e. 1/10 LC_{50}). For freshwater invertebrates (NOEC = 0.026 mg a.i./L) and fish (NOEC = 25 mg a.i./L), the RQs were 68–142 and 0.07–0.15, respectively. For the most sensitive estuarine invertebrates (NOEC = 1.05 mg a.i./L), the RQs ranged from 1.8–3.7. The assessment concluded that for freshwater aquatic invertebrates acute risk from use of methamidophos is high to very high. For marine invertebrates the risk is moderate.

4.6 Preliminary Environmental Assessment Conclusions

From an aquatic ecosystem perspective, a screening level risk assessment shows methamidophos poses a high to very high risk (RQ = 68–142) for aquatic invertebrates and a negligible risk for fish (RQ = 0.07–0.15).

For terrestrial organisms, there are high levels of acute risk for birds and mammals. While methamidophos is relatively non-persistent, there is a high chronic risk for birds (RQ = 22–64) and mammals (RQ = 26–56) due to the number and frequency of applications. A moderate risk was determined for bees (RQ = 3–7).

Mitigation of potential impacts on terrestrial ecosystems is difficult given that the non-target organisms frequent treated areas. In the case of bees, it may be possible to reduce the risk by restricting the application of methamidophos to a time when bees are not actively foraging. For birds and small mammals, there are no available options that would effectively reduce the acute risk that results from ingestion of contaminated food sources in treated areas. The chronic risk for birds and mammals can be minimized by lowering the maximum application rate and the number of applications per year.

Methamidophos can enter aquatic ecosystems through spray drift. The observance of buffer zones, however, can effectively mitigate the risk for off-site non-target organisms. Based on the spray drift predictions and the most sensitive toxicity endpoint, preliminary buffer zones (10–30 m ground applications, 35–330 m aerial applications) were calculated for mitigating the entry of methamidophos into aquatic habitats.

Methamidophos can also enter aquatic ecosystems through surface runoff. In this screening level assessment, risks were identified for aquatic invertebrates. Further refinement of the assessment is possible by refining estimates of exposure. Additional data on toxicity to aquatic invertebrates in the form of an aquatic mesocosm study (if available) could also be considered in any refinement.

5.0 Use Data and Alternatives

5.1 Alternatives to Methamidophos Use

Registered chemical alternatives to methamidophos for uses with risk concerns are listed in Appendix III. Although chemical alternatives to methamidophos are registered, the PMRA has no information on the availability and extent of use of these methods. The PMRA welcomes feedback on the availability and extent of use of the chemical alternatives to methamidophos reported in Appendix III as well as information regarding the availability, effectiveness and extent of use of non-chemical control methods for any of the registered uses.

Most non-chemical pest management practices consist of general cultural practices (including weed control, crop rotation, resistant varieties, appropriate soil cultivation and natural enemies). The PMRA identified non-chemical control measures for some of the site-pest combinations on the methamidophos labels. The effectiveness and extent of use of these non-chemical control measures have not been verified. These include the following:

- the use of sprinkler irrigation to discourage the development of diamondback larvae on Brussels sprouts;
- the use of row covers in small fields of broccoli, Brussels sprouts, cabbage and cauliflower to prevent moths from laying eggs;
- the use of plastic trenches around the perimeter of potato fields to trap overwintering adult Colorado potato beetles as they walk into a new crop field; and
- the use of propane burners to control Colorado potato beetle on small potato plants early in the season.

5.2 Value of Methamidophos

5.2.1 Aerial Application to Canola (Rapeseed) for the Control of Bertha Armyworm and Grasshoppers

Methamidophos may be applied by air to canola (rapeseed) to control grasshoppers and the bertha armyworm. Due to the nature of these pests, pesticides need to be applied to large areas in a short period of time. Furthermore, provincial monitoring for both bertha armyworm and grasshoppers is conducted.

The registered alternatives to control bertha armyworm are methomyl, chlorpyrifos, cypermethrin, lambda-cyhalothrin and deltamethrin; all are registered for ground and aerial application.

Of the registered alternatives to control grasshoppers, chlorpyrifos, dimethoate, lambda-cyhalothrin and deltamethrin are registered for ground and aerial application. Cypermethrin, carbaryl and malathion are registered for ground application only. Diazinon is registered to control grasshoppers as a non-crop land perimeter spray only (including a strip within the crop).

Limitations to the registered alternatives to methamidophos that may be applied by air are as follows.

- Deltamethrin is registered for use in the Prairie Provinces and the Peace River region of British Columbia only and is not effective at temperatures above 25°C.
- Lambda-cyhalothrin and cypermethrin are not registered to control adult grasshoppers.
- Cypermethrin is registered for aerial application to control bertha armyworm only.
- Chlorpyrifos, dimethoate and methomyl are currently under re-evaluation. Continued acceptability has not been confirmed.

5.2.2 Ground Application to Canola (Rapeseed) for the Control of Grasshoppers

Limitations to the registered alternatives to methamidophos that may be applied by ground to control grasshoppers on canola are as follows.

- Carbaryl is registered as a grasshopper bait treatment and is not as effective when alternative food sources are available (i.e. mature crops).
- Diazinon is limited to a perimeter treatment (including a strip within the crop).
- Lambda-cyhalothrin, cypermethrin and deltamethrin are not effective for grasshopper control at temperatures above 25°C.
- Lambda-cyhalothrin will not control adult grasshoppers.
- Carbaryl, chlorpyrifos, diazinon, dimethoate and malathion are currently under re-evaluation. Continued acceptability has not been confirmed.

5.2.3 Methamidophos Uses on Broccoli, Brussels Sprouts, Cabbage, Cauliflower and Potatoes

Registered alternatives from several resistance management groups exist for the purpose of rotation to delay the development of pesticide resistance.

6.0 Other Assessment Considerations

6.1 Toxic Substances Management Policy

The PMRA has taken into account the federal Toxic Substances Management Policy (TSMP) during the review of methamidophos. It has been determined that this active ingredient does not meet the TSMP cut-off criteria for the following reasons.

- The reported half-life value in water (≤8 days, anaerobic conditions), soil (≤ 0.5 and 36 days) and sediment (≤ 8 days) are below the TSMP Track 1 cut-off criteria for persistence in water (≥ 182 days), soil (≥ 182 days) and sediment (≥ 365 days).

- The reported log K_{ow} is -0.796, which is below the TSMP Track 1 cut-off criterion for bioaccumulation (≥ 5.0).

6.2 Formulant Issues

Formulant issues are being addressed through the PMRA Formulant Policy (DIR2006-02, *Formulants Policy and Implementation Guidance Document*).

7.0 Information Needed to Refine the Preliminary Risk and Value Assessment for Methamidophos

7.1 Data for refinement of Occupational Risk Assessment

Chemical-specific occupational exposure data are preferred. The type of data needed to refine the occupational exposure assessment could include, but are not limited to, the following:

- typical rate and number of applications per season;
- typical area treated per day;
- critical worker activities and their timing with respect to the stage of growth of the crop and application of methamidophos;
- passive dosimetry or biological monitoring exposure data;
- additional DFR data;
- data to support rates of application lower than the registered rates;
- information to support the feasibility of longer restricted entry intervals;
- data supporting the feasibility of additional protective clothing and/or other mitigation measures selected for postapplication worker activities; and
- data more representative of modern spray equipment and engineering controls.

7.2 Aggregate Risk Assessment

Suitable data are required to refine the acute and chronic drinking water estimated concentrations, as identified in Section 7.3. These data may allow refinements of the overall food and drinking water exposure assessment.

7.3 Data for Refinement of Environmental Assessment

For the environmental assessment, two effects studies were identified that could help in the further refinement of the risk assessment:

- an aquatic mesocosm study would provide an indication of community level effects for aquatic invertebrates; and
- additional data on the dermal toxicity of methamidophos to birds would help better characterize the potential for effects from this route of exposure for birds.

In addition, information identified for the refinement of drinking water modelling would also contribute to the refinement of surface runoff modelling. This information will help to determine the concentrations of methamidophos in non-drinking water.

It may also be possible to refine interpretation of environmental risk in a qualitative fashion through the provision of use or sales data on a regional/provincial basis.

Refinement of Drinking Water Concentrations
Further refinement of estimated concentrations in drinking water sources can be achieved by refining modelling or developing high quality monitoring data. In the case of modelling, refinements can typically be made to a number of input parameters. These can include values for fate and/or physical chemical properties, which would not affect the overall results because of the non-persistent nature of the chemical. Refinement in modelling can also be achieved with more specific information on the current use pattern (e.g. percentage of crop treated, timing of use, typical application rates used, timing of application for different crops and number of applications per year) and with proposals by registrants for potential mitigation such as changes to rates and frequencies of applications.

Another option for refinements is by using confirmatory surface water monitoring data to evaluate actual acute and chronic concentrations of methamidophos in the drinking water sources. Monitoring information would need to be generated from a multiyear sampling programme involving Canadian community reservoir water systems and dugouts from surface water sources in multiple agricultural locations to represent different use sites, crops, soil types and rainfall regimes selected from areas where methamidophos is used. The registrant would be required to submit a draft protocol for review and comments to ensure that the sampling locations, sampling times and procedures are sufficient to assess the drinking water concerns.

It may also be possible to refine interpretation of risk in a qualitative fashion through the provision of use or sales data on a regional/provincial basis.

7.4 Data for Refinement of Value Assessment

The PMRA welcomes feedback on the availability and extent of use of chemical alternatives to methamidophos. The PMRA also welcomes information regarding the availability, effectiveness and extent of use of non-chemical pest management practices methods for any of the registered uses.

List of Abbreviations

°C	degree Celsius
µg	microgram
ADI	acceptable daily intake
A.L.	active ingredient
ARfD	acute reference dose
ARI	aggregate risk index
atm	atmosphere(s)
BChE	brain cholinesterase
bw	body weight
CAS	Chemical Abstracts Service
cm^2	centimetre(s) squared
DEEM®	Dietary Exposure Evaluation Model
DFR	dislodgeable foliar residue
DWLOC	drinking water level of comparison
EC_{50}	effect concentration 50%
EChE	erythrocyte cholinesterase
EXAMS	Exposure Analysis Modeling System
F_0	parental generation
F_1	first filial generation
g	gram(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient [there are many different ways of presenting this one]
L	litre(s)
LEACHM	Leaching Estimation and Chemistry Model
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOAEL	lowest observed adverse effect level
m^3	metre(s) cubed
mg	milligram(s)
MOE	margin of exposure
mol	mole
N	nursing
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NP/NN	not pregnant, not nursing
NTE	neuropathy target esterase
PChE	plasma cholinesterase
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database

PMRA	Pest Management Regulatory Agency
P/NN	pregnant, not nursing
PPE	personal protective equipment
PRZM	Pesticide Root Zone Model
RED	Reregistration Eligibility Decision
RfD	reference dose
REI	restricted-entry interval
RI	risk index
RQ	risk quotient
SF	safety factor
TC	transfer coefficient
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
USEPA	United States Environmental Protection Agency

Appendix I Methamidophos Products Currently Registered (excluding discontinued products or products with a submission for discontinuation) as of 1 November 2005

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
28157	Technical	Bayer Cropsciences Inc.	Methamidophos Technical Insecticide	Solid	75% nominal
25370	Technical	Bayer Cropsciences Inc.	Monitor Technical Insecticide	Solid	77% nominal
25369	Technical	Arysta Lifescience Corporation	Methamidophos (Monitor) Technical	Solid	77% nominal
12434	Restricted	Arysta Lifescience Corporation	Monitor 480 Liquid Insecticide	Solution	480 g a.i./L nominal
12287	Restricted	Bayer Cropsciences Inc.	Monitor 480 Liquid Insecticide	Solution	480 g a.i./L nominal

Appendix II Registered Canadian Uses of Methamidophos

Site(s)	Pests(s)	Application Methods and Equipment	Application Rate (g a.i./ha)		Maximum number of applications per year	Minimum number of days between applications
			Maximum single	Maximum cumulative		
Use-Site Category 7—Industrial Oilseed Crops Use-Site Category 13—Terrestrial Feed Crops Use-Site Category 14—Terrestrial Food Crops						
Canola (rapeseed)	Bertha armyworm, Grasshoppers	Conventional ground application equipment: hydraulic sprayers	600	1200	2	Not stated on the label.
		Aerial application equipment				
Use-Site Category 14–Terrestrial Food Crops						
Broccoli, Brussels sprouts, Cabbage, Cauliflower	Cabbage looper, Imported cabbageworm, Diamondback moth (larvae), Aphids	Conventional ground application equipment: hydraulic sprayers	1104	Not able to calculate as the maximum number of applications is not specified on the label.	Not stated on the label.	7
Head lettuce (field grown)	Cabbage looper, Aphids					
Potato	Aphids, Colorado potato beetle, Potato flea beetle, Potato leafhopper, Tarnished plant bug (Ontario only)					10

Two Restricted Class products, Registration Number 12287 and 12434 formulated as solutions as of 1 November 2005. All uses are supported by the registrants.

Appendix III Alternative Registered Active Ingredients for Those Site-Pest Combinations of Methamidophos for Which Both Environmental and Worker Risk Concerns Have Been Identified

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (resistance management group number.)[2, 3]
Use-Site Category 7—Industrial Oilseed Crops Use-Site Category 13—Terrestrial Feed Crops Use-Site Category 14—Terrestrial Food Crops			
Canola (rapeseed)	Bertha armyworm	Major pest Canada: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure.	1A: Methomyl[4] 1B: Chlorpyrifos[4] 3: Cypermethrin, Deltamethrin[5], Lambda-cyhalothrin
	Grasshoppers		1A: Carbaryl[4] (bait treatment) 1B: Diazinon[6], Chlorpyrifos[4], Dimethoate[4], Malathion[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin[5]
Use-Site Category 14—Terrestrial Food Crops			
Broccoli	Cabbage looper	Major pest British Columbia: Widespread yearly occurrence with high pest pressure. Ontario, Quebec: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. New Brunswick, Newfoundland, Labrador: No data	1A: Carbaryl[4], Methomyl[4] 1B: Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Imported cabbageworm	Major pest British Columbia, Ontario: Widespread yearly occurrence with high pest pressure. Quebec: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. New Brunswick, Newfoundland, Labrador: No data	1A: Carbaryl[4], Methomyl[4] 1B: Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Diamondback moth (larvae)	Major pest British Columbia, Ontario, Quebec: Widespread yearly occurrence with high pest pressure. New Brunswick, Newfoundland, Labrador: No data	1A: Carbaryl[4], Methomyl[4] 1B: Azinphos-methyl[7], Diazinon[4], Naled[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (resistance management group number.)[2, 3]
	Aphids	Major pest British Columbia: Widespread yearly occurrence with high pest pressure. Ontario, Quebec:Widespread yearly occurrence with low to moderate pest pressure. New Brunswick, Newfoundland, Labrador: No data	1B: Diazinon[4], Dimethoate[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 4: Acetamiprid Other: Insecticidal soap[8], Insecticidal soap[8] + Pyrethrin
Brussels sprouts	Cabbage looper	No data	1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Imported cabbageworm		1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4], Trichlorfon[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Diamondback moth (larvae)		1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Naled[4], Trichlorfon[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Aphids		1B: Acephate[4, 9], Malathion[4], naled[4] 2A: Endosulfan[4] 4: Acetamiprid, Imidacloprid (Green peach and Cabbage aphid only) Other: Insecticidal soap[8], Insecticidal soap[8] + Pyrethrin
Cabbage	Cabbage looper	Major pest British Columbia: Widespread yearly occurrence with high pest pressure. Ontario, Quebec: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. Nova Scotia: Widespread yearly occurrence with low to moderate pest pressure. Manitoba, New Brunswick, Prince Edward Island, Newfoundland, Labrador: No data	1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (resistance management group number.)[2, 3]
	Imported cabbageworm	Major pest British Columbia, Ontario, Nova Scotia: Widespread yearly occurrence with high pest pressure. Quebec: Widespread yearly occurrence with low to moderate pest pressure. Manitoba, New Brunswick, Prince Edward Island, Newfoundland, Labrador: No data	1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4], Trichlorfon[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Diamond-back moth (larvae)	Major pest British Columbia, Ontario, Nova Scotia: Widespread yearly occurrence with high pest pressure. Quebec: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. Manitoba, New Brunswick, Prince Edward Island, Newfoundland, Labrador: No data	1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Naled[4], Trichlorfon[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Aphids	Major pest British Columbia: Widespread yearly occurrence with high pest pressure. Ontario, Quebec: Widespread yearly occurrence with low to moderate pest pressure. Nova Scotia: Localized yearly occurrence with low to moderate pest pressure or widespread sporadic occurrence with low to moderate pest pressure. Manitoba, New Brunswick, Prince Edward Island, Newfoundland, Labrador: No data	1B: Acephate[4, 9], Diazinon[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 4: Acetamiprid Other: Insecticidal soap[8], Insecticidal soap[8] + Pyrethrin
Cauliflower	Cabbage looper	No data	1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Malathion[4], Naled[4], trichlorfon[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]
	Imported cabbageworm		
	Diamond-back moth (larvae)		1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Naled[4], Trichlorfon[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 5: Spinosad 11: *Bacillus thuringiensis* var *kurstaki*[4]

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (resistance management group number.)[2, 3]
	Aphids	No data	1B: Acephate[4, 9], Diazinon[4], Dimethoate[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 4: Acetamiprid Other: Insecticidal soap[8], Insecticidal soap[8] + Pyrethrin
Head lettuce	Cabbage looper	No data	1A: Carbaryl[4], Methomyl[4] 1B: Acephate[4] (crisphead lettuce only), Diazinon[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin 5: Spinosad 11:*Bacillus thuringiensis* var *kurstaki*[4]
	Aphids	No data	1A: Pirimicarb (Green peach, Potato, Lettuce and Foxglove aphid only) 1B: Acephate[4] (Green peach aphid on Head lettuce only), Diazinon[4], Dimethoate[4], Malathion[4], Naled[4] 2A: Endosulfan[4] 4: Acetamiprid, Imidacloprid (Lettuce aphid only) Other: Insecticidal soap[8], Insecticidal soap[8] + Pyrethrin
Potato	Aphids	Major pest British Columbia, Prince Edward Island: Widespread yearly occurrence with high pest pressure. Alberta, Saskatchewan, Quebec: Widespread yearly occurrence with low to moderate pest pressure. Manitoba, Ontario, Nova Scotia: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. Newfoundland, Labrador: Localized yearly occurrence with low to moderate pest pressure or widespread sporadic occurrence with low to moderate pest pressure.	1A: Methomyl[4], Pirimicarb, Oxamyl[4, 10] 1B: Acephate[4, 10], Diazinon[4], Dimethoate[4], Malathion[4], Phosmet[4] (Potato aphid only) 2A: Endosulfan[4] 3: Deltamethrin[11] 4: Acetamiprid, Imidacloprid 9B: Pymetrozine Other: Insecticidal soap[8], Insecticidal soap[8] + Pyrethrin

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (resistance management group number.)[2, 3]
	Colorado potato beetle	Major pest British Columbia: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. Alberta, Saskatchewan: Widespread yearly occurrence with low to moderate pest pressure. Manitoba, Ontario, Quebec, New Brunswick, Nova Scotia, Prince Edward Island: Widespread yearly occurrence with high pest pressure. Newfoundland, Labrador: pest not present	1A: Carbaryl[4], Carbofuran[4], Oxamyl[4] 1B: Azinphos-methyl[7], Chlorpyrifos[4], Diazinon[4], Malathion[4], Naled[4], Phosmet[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 4: Acetamiprid, Imidacloprid 5: Spinosad 11: *Bacillus thuringiensis* var *tenebrionis*[4] 17: Cyromazine (Ontario, Quebec and Atlantic provinces only)
	Potato flea beetle	Major pest British Columbia: pest not present Alberta, Newfoundland, Labrador: Localized yearly occurrence with low to moderate pest pressure or widespread sporadic occurrence with low to moderate pest pressure. Saskatchewan, Manitoba, New Brunswick: Widespread yearly occurrence with low to moderate pest pressure. Ontario, Quebec: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure. Nova Scotia, Prince Edward Island: Widespread yearly occurrence with high pest pressure.	1A: Carbaryl[4], Carbofuran[4], Methomyl[4], Oxamyl[4] 1B: Acephate[4], Azinphos-methyl[7], Chlorpyrifos[4], Diazinon[4], Naled[4], Phosmet[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 4: Imidacloprid

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (resistance management group number.)[2, 3]
	Potato leafhopper	Major pest British Columbia, Saskatchewan, Manitoba, New Brunswick, Prince Edward Island, Newfoundland, Labrador: Localized yearly occurrence with low to moderate pest pressure or widespread sporadic occurrence with low to moderate pest pressure. Alberta: Widespread yearly occurrence, low to moderate pest pressure. Ontario: Widespread yearly occurrence with high pest pressure. Quebec, Nova Scotia: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure.	1A: Carbaryl[4], Carbofuran[4], Methomyl[4], Oxamyl[4] 1B: Acephate[4], Azinphos-methyl[7], Diazinon[4], Dimethoate[4], Malathion[4], Naled[4], Phosmet[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin 4: Imidacloprid
	Tarnished plant bug (Ontario only)	Major pest British Columbia, Alberta, Saskatchewan, Quebec: Widespread yearly occurrence with low to moderate pest pressure. Manitoba, New Brunswick, Newfoundland, Labrador: Localized yearly occurrence with low to moderate pest pressure or widespread sporadic occurrence with low to moderate pest pressure. Ontario, Nova Scotia, Prince Edward Island: Localized yearly occurrence with high pest pressure or widespread sporadic occurrence with high pest pressure.	1A: Carbaryl[4], Carbofuran[4], Oxamyl[4] 1B: Acephate[4], Azinphos-methyl[7], Chlorpyrifos[4], Dimethoate[4] 2A: Endosulfan[4] 3: Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin

1 Pest status and incidence data from the Agriculture and Agri-Food Canada crop profiles.

2 This is a list of registered options as of 1 November 2005. The PMRA does not endorse any of the options listed.

3 Insecticide and Acaricide Resistance Management Group Numbers based upon DIR99-06 *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*:1A = acetylcholinesterase inhibitors (carbamates); 1B = acetylcholinesterase inhibitors (organophosphates); 2A = gamma-aminobutyric acid (GABA) gated chloride channel antagonists (chlorinated cyclodienes or polychlorocycloalkanes); 3 = sodium channel modulators (diphenylethanes or synthetic pyrethroids or pyrethrins); 4 = acetylcholine receptor agonists/antagonists (chloronicotines or nicotine or cartap or bensultap); 5 = acetylcholine receptor modulators (spinosyns); 9B = compounds of unknown or non-specific site of action (feeding disruptors; pymetrozine or cryolite); 11 = microbial disruptors of insect mid-gut membranes (*Bacillus thuringiensis* microbials); 17 = inhibit chitin biosynthesis type
2- Dipteran (triazine).

4 These active ingredients are under re-evaluation.

5 Use is limited to the Prairie provinces and Peace River region of British Columbia only.

6 Diazinon is registered as a border spray only (including a strip within the crop).

7 The re-evaluation of azinphos-methyl is complete. All uses of azinphos-methyl are proposed to be phased out as outlined in RRD2004-05, *Azinphos-methyl*.

8 Re-evaluation of insecticidal soap is complete (RRD2004-26, *Soap Salts*).

9 Registered to control green peach aphid only.

10 Registered to control green peach aphid and potato aphid only.

11 For control of potato aphid and buckthorn aphid in eastern Canada and British Columbia only.

Appendix IV Toxicology Endpoints for Health Risk Assessment for Methamidophos

Exposure Scenario	Dose (mg/kg bw/day)	Endpoint	Study	UF/SF or MOE[c]
Acute Dietary	NOAEL = 0.3	Brain, erythrocyte and plasma cholinesterase inhibition	Acute Neurotoxicity—Rat	300
	ARfD = 0.001 mg/kg bw			
Chronic Dietary	NOAEL = 0.03	Brain, erythrocyte and plasma cholinesterase inhibition	8-Week Oral Toxicity—Rat	300
	ADI = 0.0001 mg/kg bw/day			
Short-Term[a] Dermal	Dermal NOAEL = 0.75	Brain, erythrocyte and plasma cholinesterase inhibition	3-Week Dermal Toxicity—Rat	300
Intermediate-Term[b] Dermal	Dermal NOAEL = 0.75	Brain, erythrocyte and plasma cholinesterase inhibition	3-Week Dermal Toxicity—Rat	300
Short-Term[a] Inhalation	Inhalation NOAEL = 0.53	Brain, erythrocyte and plasma cholinesterase inhibition	3-Week Inhalation Toxicity—Rat	300
Intermediate-Term[b] Inhalation	Inhalation NOAEL = 0.27	Brain, erythrocyte and plasma cholinesterase inhibition	13-Week Inhalation Toxicity—Rat	300
Aggregate[a]	Oral NOAEL = 0.03 Dermal NOAEL = 0.75	Brain, erythrocyte and plasma cholinesterase inhibition	8-Week Oral Toxicity—Rat 3-Week Dermal Toxicity—Rat	300

[a] Duration of exposure is 1–30 days

[b] Duration of exposure is 1–6 months

[c] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to desired MOE for occupational or residential assessments

Appendix V Occupational Risk Estimates for Methamidophos

Table 1 Route-Specific MOEs for Mixer/Loaders and Applicators (short-term duration)

Crop	Application Method	Rate (kg a.i./ha)	Area Treated (ha/day)	Dermal MOEs[a]			Inhalation MOEs[b]			Combined MOEs[c]		
				Min PPE[d]	Max PPE[e]	EC[f]	No Respirator	Respirator	EC[f]	Min PPE[d] Respirator	Max PPE[d] Respirator	EC[f]
Mixer/Loader/Applicator												
Cole crops	Groundboom	1.1	32	28	31	50	410	4102	6177	27	31	49
Lettuce	Groundboom	1.1	32	28	31	50	410	4102	6177	27	31	49
Potatoes	Groundboom (farmer)	1.1	80	11	12	20	164	1641	2471	11	12	20
	Groundboom (custom)		300	3	3	5	44	438	659	3	3	5
Canola	Groundboom (farmer)	0.6	150	11	12	19	161	1610	2425	11	12	19
	Groundboom (custom)		300	5	6	10	81	805	1212	5	6	10
	Aerial (mixer/loader)	0.6	490	N/A		9	N/A		1147	N/A		9
	Aerial (applicator)					18			1147			18

Shaded cells in the table are below the target MOE.

[a] Dermal MOE = $\frac{\text{dermal NOAEL}}{\text{dermal exposure}}$. The short- and intermediate-term dermal NOAEL is 0.75 mg/kg body weight/day. The target dermal MOE is 300.

[b] Inhalation MOE = $\frac{\text{inhalation NOAEL}}{\text{inhalation exposure}}$. The short-term inhalation NOAEL is 0.53 mg/kg body weight/day. The target inhalation MOE is 300.

[c] Combined MOE = $\frac{1}{1/MOE_{dermal} + 1/MOE_{inhalation}}$

[d] Min PPE = minimum PPE = coveralls over single layer, gloves and respirator

[e] Max PPE = maximum PPE = chemical-resistant coveralls over single layer, gloves and respirator

[f] EC = engineering controls; mixing loading EC = water-soluble packaging, single layer plus gloves; applying EC = closed cab and single layer clothing

N/A = not available

Table 2 Route-Specific MOEs for Mixer/Loaders and Applicators (intermediate-term duration)

Crop	Application Method	Rate (kg a.i./ha)	Area Treated (ha/day)	Dermal MOEs[a]			Inhalation MOEs[b]			Combined MOEs[c]		
				Min PPE[d]	Max PPE[e]	EC[f]	No Respirator	Respirator	EC[f]	Min PPE[d] Respirator	Max PPE[d] Respirator	EC[f] Respirator
Mixer/Loader/Applicator												
Cole crops	Groundboom	1.1	32	28	31	50	209	2090	3147	27	31	49
Lettuce	Groundboom	1.1	32	28	31	50	209	2090	3147	27	31	49
Potatoes	Groundboom (farmer)	1.1	80	11	12	20	84	836	1259	11	12	20
	Groundboom (custom)		300	3	3	5	22	223	336	3	3	5
Canola	Groundboom (farmer)	0.6	150	11	12	19	82	820	1235	11	12	19
	Groundboom (custom)		300	5	6	10	41	410	618	5	6	10
	Aerial (mixer/loader)	0.6	490	N/A		9	N/A		584	N/A		9
	Aerial (applicator)					18			584			18

Shaded cells in the table are below the target MOE.

[a] Dermal MOE = $\frac{\text{dermal NOAEL}}{\text{dermal exposure}}$. The short- and intermediate-term dermal NOAEL is 0.75 mg/kg body weight/day.
The target dermal MOE is 300.

[b] Inhalation MOE = $\frac{\text{inhalation NOAEL}}{\text{inhalation exposure}}$. The intermediate-term inhalation NOAEL is 0.27 mg/kg body weight/day.
The target inhalation MOE is 300.

[c] Combined MOE = $\frac{1}{1/MOE_{dermal} + 1/MOE_{inhalation}}$

[d] Min PPE = minimum PPE = coveralls over single layer, gloves and respirator

[e] Max PPE = maximum PPE = chemical-resistant coveralls over single layer, gloves and respirator

[f] EC = engineering controls; mixing loading EC = water soluble packaging, single layer plus gloves; applying EC = closed cab and single layer clothing

N/A = not available

Appendix VI Postapplication Exposure Estimates, SRLs and REIs for Methamidophos

Table 1 Postapplication Exposure Estimates, SRLs and REIs

Crop	Activity	Transfer Coefficient (cm^2/hr)[a]	Max. Application Rate (kg a.i./ha)	Safe Residue Limit[b, c, d] ($\mu g/cm^2$)	Day 0 DFR Value	Proposed REI[d] (days)
Field/row crop low, medium						
Canola	Scouting (full foliage)	1500	0.6	0.0146	0.2639[f]	14
	Scouting (low foliage)	100		0.2188	0.2639[f]	1
Vegetable, root						
Potato	Irrigation, scouting (full foliage)	1500	1.1	0.0146	0.4839	17
	Hand weeding, irrigating, scouting (low foliage)	300		0.0729	0.4839	9
Vegetables head and stem *(Brassica)*						
Broccoli, Cabbage, Cauliflower, Brussel sprouts	Hand harvest, irrigation, pruning, topping, thinning, tying	5000	1.1	0.0044	0.4839	22
	Scouting	4000		0.0055	0.4839	21
	Hand weeding	2000		0.0109	0.4839	18
	Scouting, thinning, hand weeding, hand pruning, irrigation (low foliage)	2000		0.0109	0.4839	18
	Mechanical harvesting	Special concern[e]				
Vegetables leafy						
Lettuce	Hand harvesting	2500	1.1	0.0088	0.4839	19
	Irrigation, scouting (full foliage)	1500		0.0146	0.4839	17
	Hand weeding, irrigating, scouting, thinning (low foliage)	500		0.0438	0.4839	12

[a] Transfer coefficients are from the Science Advisory Council for Exposure Agricultural Transfer Coefficient document (USEPA 2000).

[b] Safe residue limit = (NOAEL × bw / dermal absorption) / (TC × exposure time (hour) × SF).

[c] Based on the short and intermediate term NOAEL of 0.75 mg/kg/day with a target of 300.

[d] REI is the day when the DFR value is less than or equal to the safe residue limit.

[e] This activity was identified to be of special concern because significant contact is known to occur with this crop. However, this activity is commonly identified as a non-contact activity with other crops.

[f] The DFR data was adjusted for the different application rate for canola.

Appendix VII Dietary and Aggregate Exposure Estimates for Methamidophos

Table 1 Summary of Dietary Exposure and DWLOC Estimates for Methamidophos

	Acute Exposure (99.9th percentile)		Chronic Exposure		DWLOC[1] (µg/L)	
Population groups	**mg/kg bw/day**	**% of ARfD**	**mg/kg bw/day**	**% of ADI**	**Acute**	**Chronic**
General Population (total)	0.000533	53.3	0.000029	29.2	16.3	2.5
General Population (spring)	0.0005	54.1	0.000029	28.8	16.1	2.5
General Population (summer)	0.0006	56.2	0.000031	31.4	15.3	2.4
General Population (autumn)	0.000517	51.7	0.000028	28.3	16.9	2.5
General Population (winter)	0.000507	50.7	0.000028	28.4	17.3	2.5
Northeast region	0.000558	55.9	0.000030	30.0	15.5	2.5
Midwest region	0.000537	53.7	0.000031	30.8	16.2	2.4
Western region	0.000603	60.4	0.000030	29.7	13.9	2.5
All infants (< 1 year)	0.000304	30.4	0.000043	42.5	7.0	0.6
Nursing infants	0.000217	21.7	0.000019	18.6	7.8	0.8
Non-nursing infants	0.000334	33.4	0	51.6	6.7	0.5
Children 1–6 years	0.000754	75.4	0.000054	54.5	3.7	0.7
Children 7–12 years	0.000565	56.5	0.000036	36.1	8.5	1.2
Females 13–9 NP/NN	0.000556	55.6	0.000024	23.8	13.8	2.4
Females 20+ NP/NN	0.000581	58.1	0.000025	24.8	13.0	2.3
Females 13-50 years	0.000460	46.1	0.000025	24.7	16.7	2.3
Females 13+ P/NN	0.000528	52.8	0.000024	23.7	14.6	2.4
Females 13+ N	0.000529	52.9	0.000024	24.4	14.6	2.4
Males 13–19 years	0.000430	43.0	0.000026	26.4	20.0	2.6
Males 20+ years	0.000489	48.9	0.000026	25.9	17.9	2.6
Seniors 55+ years	0.000491	49.1	0.000025	24.5	17.8	2.6

[1] Where DWLOC = (RfD-dietary exposure) × (bw) / (water consumption)
Daily water intake: infants and children = 1 L; all other population subgroups = 2 L
Body weight: adult and male populations = 70 kg; adult female populations = 62 kg; all infants = 10 kg; children 1–6 years = 15 kg; children 7–12 years = 39 kg

NP/NN not pregnant, not nursing
P/NN pregnant, not nursing
N nursing

Table 2 Short-Term Aggregate Exposure Estimates for Methamidophos for Entry in Treated Orchards

Age Group	Food[1] µg/kg/day (MOE)	Entry to Treated Ornamentals µg/kg/day (MOE)	Aggregate MOE[2] Excluding Drinking Water	Aggregate RI[3] Excluding Drinking Water	Aggregate DWLOC[4] µg/L
		dermal[5]			
Adults 70 kg	0.031 (968)	1.59 (472)	317	1.06	0.19
Youth 39 kg	0.036 (833)	1.42 (528)	323	1.08	0.14

1 Based on chronic dietary exposure estimates generated using from Appendix IV.

2 Aggregate MOE = 1/ ($1/MOE_{oral}$ + $1/MOE_{dermal}$).

3 Aggregate RI = 1/ ($1/RI_{oral}$ + $1/RI_{dermal}$); an ARI of 1.00 or greater is not of concern.

4 Where DWLOC = (RfD-non-drinking water exposure) × (bw) / (water consumption). Consumption and body weights as per Appendix IV.

5 Based on two annual applications of acephate at the label rate of 637.5 g A.L. of soluble powder per 1000 L of water. Reentry exposure was determined based on a DFR of 0.13% and TC of 10 000 and 5000 cm^2/hour for adults and youth, respectively.