PRVD2009-07

Proposed Re-evaluation Decision

Phenmedipham

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Overview

What Is the Proposed Re-evaluation Decision?

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

An evaluation of available scientific information found that products containing phenmedipham do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of phenmedipham uses, new risk-reduction measures must be included on the labels of all products. No additional data are being requested at this time.

Phenmedipham end-use products that contain more than one active ingredient under re-evaluation will be eligible for continued registration only when all of those other active ingredients are determined to be eligible.

This proposal affects all end-use products containing phenmedipham registered in Canada. Once the final Re-evaluation Decision is made, the registrants will be instructed on how to address any new requirements.

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

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

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications.

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

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

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

Phenmedipham, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

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

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

Based on the health and environmental risk assessments published in a 2005 RED, the USEPA concluded that phenmedipham was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the United States and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian Re-evaluation Decision.

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

What Is Phenmedipham?

Phenmedipham is a selective systemic herbicide that is used to control broad-leaved weeds in sugarbeets. Phenmedipham is applied using ground equipment, by farm workers and professional (custom) applicators.

Health Considerations

Can Approved Uses of Phenmedipham Affect Human Health?

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

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

The USEPA concluded that phenmedipham was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are currently in place in Canada.

Maximum Residue Limits

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

Phenmedipham is currently registered in Canada for use on sugarbeets and could be used in other countries on crops that are imported into Canada. No specific MRLs have been established for phenmedipham in Canada. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

Environmental Considerations

What Happens When Phenmedipham Is Introduced Into the Environment?

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

Non-target organisms (e.g. birds, mammals, insects, aquatic organisms and terrestrial plants) could be exposed to phenmedipham in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the estimated environmental concentration to the relevant effects endpoint of concern. The resulting risk quotients are compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a negligible risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some degree of risk.

The USEPA concluded that the reregistration of phenmedipham was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation. The PMRA will require aquatic and terrestrial buffer zones for phenmedipham to protect aquatic organisms and terrestrial plants from spray drift.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of phenmedipham, the PMRA is proposing further risk-reduction measures for product labels.

Environment

- Buffer zones to protect non-target, sensitive aquatic and terrestrial habitats.

Next Steps

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

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

Science Evaluation

1.0 Introduction

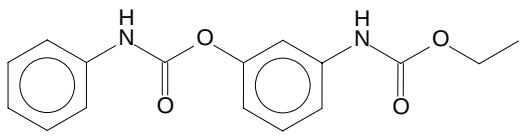
Phenmedipham is a selective systemic herbicide absorbed through the leaves, with translocation primarily in the apoplast, which acts by inhibiting photosynthetic electron transport at the photosystem II receptor site.

Following the re-evaluation announcement for phenmedipham, the registrant of the technical grade active ingredient in Canada indicated continued support for all uses included on the labels of commercial end-use products in Canada.

The PMRA used recent assessments of phenmedipham from the USEPA. The USEPA RED document for phenmedipham dated from 2005, as well as other information on the regulatory status of phenmedipham in the United States that can be found on the USEPA Pesticide Registration Status page.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Phenmedipham
Function	Herbicide
Chemical family	Carbamates
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	3-methyoxycarbonylaminophenyl 3-methylcarbanilate
2 Chemical Abstracts Service (CAS)	3-[(methoxycarbonyl)amino]phenyl (3-methylphenyl)carbamate
CAS Registry Number	13684-63-4
Molecular formula	$C_{16}H_{16}N_2O_4$
Structural formula	
Molecular weight	300.3 amu

Purity of the technical grade active ingredient	97.5% NS
Registration Number	19204

Based on the manufacturing process, the product is not expected to contain impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Volume 13, SI/2008-67 (2008-06-25), including TSMP Track 1 substances.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure	$\leq 1 \times 10^{-6}$ mmHg
Solubility in water	1–10 ppm
n-Octanol–water partition coefficient	Log $K_{ow} \geq 3$
Dissociation constant	p*K*a < normal pH

2.3 Comparison of Use Patterns in Canada and the United States

Phenmedipham is a selective systemic herbicide registered in Canada to control broad-leaved weeds. It acts by inhibiting photosynthetic electron transport at the photosystem II receptor site. It is used on sugarbeets. It is applied after the emergence of weeds (postemergence).

The end-use products containing phenmedipham registered in Canada are co-formulated with desmedipham as emulsifiable concentrates. Phenmedipham can be applied using field sprayers, with a maximum seasonal application rate of 1.26 kg a.i./ha, as follows:

- in a single application at a maximum rate of 0.73 kg a.i./ha, past the 2-true leaf stage. A second application can be made at a maximum rate of 0.53 kg a.i./ha, with an application interval of at least seven days; or

- in split applications (maximum of two applications) at a maximum rate of 0.27 kg a.i./ha per application, at any growth stage, with an application interval of five to seven days between the two applications.

The United States and Canadian use patterns were compared. Based on the comparison of formulation types, use sites, guarantees, application methods and application rates for phenmedipham, as they appear on the current Canadian labels and as described in the USEPA RED, the following can be observed.

- The Canadian formulation types, application methods, and use site (i.e. only on sugarbeets) are among those registered in the United States. Other uses of phenmedipham that are registered in the United States, but not in Canada, include garden and table beets, spinach and Swiss chard for seed production.

- The maximum Canadian application rate (0.73 kg a.i./ha) is comparable to the maximum application rate for sugarbeets (0.71 kg a.i./ha) in the United States, whereas the maximum application rate for garden beets and spinaches (1.09 kg a.i./ha) in the United States is higher. The maximum Canadian application rate per season (1.26 kg a.i./ha/season) is also similar to the maximum application rate per season (1.13 kg a.i./ha/season) in the United States

Based on this comparison of use patterns, it was concluded that the USEPA RED for phenmedipham is an adequate basis for the re-evaluation of uses of this chemical in Canada.

All current uses are being supported by the registrant and were, therefore, considered in the re-evaluation of phenmedipham. Appendix I lists all phenmedipham products that are registered as of 8 December 2008, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 2005 RED, the USEPA concluded that the end-use products formulated with phenmedipham met the safety standard under the American *Food Quality Protection Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended product labels.

3.1 Human Health

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

In Canada, exposure to phenmedipham may occur through consumption of food and water, while working as a mixer/loader/applicator or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix II.

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). 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 that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Workers can be exposed to phenmedipham when mixing, loading or applying the pesticide and when entering a treated site to conduct activities such as scouting and/or handling of treated crops.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

Short- and intermediate-term dermal and inhalation endpoints of concern were identified by the USEPA. Based on the use pattern, the USEPA did not expect long-term (> 6 months) occupational exposure for phenmedipham. Phenmedipham was classified as "not likely to be a human carcinogen". On this basis, long-term dermal and inhalation, and cancer risk assessments were not conducted.

Three combined dermal and inhalation exposure scenarios for mixers, loaders, applicators, and other handlers were identified by the USEPA. Among the exposure scenarios assessed in the RED, the following two were considered relevant to the Canadian situation:

- mixing/loading liquid formulations for groundboom applications; and
- applying sprays for groundboom applications.

Handler exposure analyses were performed using the Pesticide Handlers Exposure Database (PHED) assuming baseline personal protective equipment (PPE) (i.e. long pants, long-sleeved shirt, shoes plus socks) for application, and baseline personal protective equipment plus chemical-resistant gloves for mixing/loading. Short- (< 30 days) and intermediate-term (1–6 months) dermal and inhalation risks were based on the maximum phenmedipham application rate of 1.12 kg a.i./ha, an oral no observed adverse effect level (NOAEL) of 24 mg/kg/day from a combined chronic toxicity/cancer study in the rat, and the assumptions that the dermal and inhalation absorption rates are 10% and 100%, respectively. Other assumptions included a default body weight of 70 kg, an eight hour work day and a daily treated area of approximately 32 ha/day.

The USEPA reported acceptable short- and intermediate-term dermal and inhalation combined MOEs for all occupational exposure scenarios, ranging from 6000 to 9800 (target MOE = 100). Based on this, and given that United States phenmedipham product labels currently require baseline personal protective equipment (i.e. long pants, long-sleeved shirt, shoes plus socks)

with chemical-resistant gloves, no additional mitigation measures were required with respect to occupational handler exposure by the USEPA.

The RED adequately addressed exposure scenarios associated with the uses of products containing phenmedipham in Canada, and conclusions derived from the RED apply to the Canadian situation. Canadian phenmedipham end-use product labels currently require baseline personal protective equipment for mixing, loading, application, cleanup and repair and chemical-resistant gloves for mixing and loading. Therefore, no additional mitigation measure is required by the PMRA to further protect handlers.

3.1.1.2 Post-application Exposure and Risk

The USEPA considers that inhalation exposure is negligible in outdoor post-application scenarios, since the dilution factor outdoors is considered ‘‘infinite’’ and also because phenmedipham has a low vapour pressure; Therefore, no post-application occupational risk assessment was conducted for this route of exposure.

The post-application occupational risk assessment considered short- (≤30 days) and intermediate-term (1–6 months) dermal exposures to workers entering treated sites. Based on phenmedipham’s use pattern, workers could be exposed to residues after the product is applied. Four scenarios were identified in the RED, and considered relevant to the Canadian situation; irrigation, scouting, hand-weeding, and thinning.

Chemical-specific dislodgeable foliar residue (DFR) default values and activity-specific transfer coefficients (TC) were used to analyze post-application exposure from contact with treated foliage at various times after treatment. DFR data include the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant. No chemical-specific DFR data was available; Therefore, DFR estimates based on standard assumptions were used in the assessment. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late season cotton) and reflect standard work clothing worn by adult agricultural workers. Assumptions used in the risk assessment included exposure following application at 0.71 kg a.i./ha, a default body weight of 70 kg and an eight hour work day.

MOEs of concern were calculated for irrigation, scouting, hand-weeding and thinning activities and acceptable MOEs ranging from 1100 to 16 000 were found at day zero (assuming a restricted-entry interval (REI) of 12 hours after application). Based on this, the USEPA required the default 12-hour REI imposed by the United States Worker Protection Standard for Agricultural Pesticides be retained.

The RED adequately addressed exposure scenarios associated with the Canadian uses of phenmedipham, and conclusions derived from the RED are considered to be applicable to the Canadian situation. Canadian labels currently require a 24-hour REI (due to the fact that Canadian end-use products are co-formulated with another active ingredient, desmedipham); therefore, no additional mitigation measure is required by the PMRA to further protect workers from post-application exposure.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

No residential uses are registered in the United States or Canada. Thus, no residential exposure is expected and, therefore, a residential risk assessment was not conducted.

3.1.2.2 Exposure from Food

No acute end-point of concern was identified by the USEPA and phenmedipham was classified as "not likely to be a human carcinogen". On this basis, acute and cancer risk assessments were not conducted.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the Acceptable Daily Intake (ADI) in Canada, and, in the RED, it is expressed as the chronic population adjusted dose (cPAD). The Acceptable Daily Intake is based on a relevant endpoint from toxicology studies and on safety and *Pest Control Products Act* factors protective of the most sensitive subpopulation (see Appendix II).

Chronic dietary (food) exposure assessments were conducted for phenmedipham using Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), resulting in < 1% of the cPAD for the United States general population and all subgroups. The assessment was based on a cPAD of 0.24 mg a.i./kg bw/day, which was calculated based on a combined chronic toxicity/cancer rat study (no observed adverse effect level [NOAEL] = 24 mg a.i./kg bw/day) and an uncertainty factor of 100-fold. It was assumed that 100% of each commodity was treated and that all residues were at established United States tolerance levels. The USEPA considered the estimated chronic exposure to phenmedipham from food to be below its level of concern.

This assessment is considered to be relevant to Canada because it included the use registered in Canada (i.e. sugarbeets), the tolerances used for sugarbeets were higher than the 0.1 ppm general MRL[3] that applies in Canada for phenmedipham, and it was based on conservative assumptions. Therefore, the USEPA's assessment is considered applicable to the Canadian situation and no additional mitigation measures are required with respect to exposure through food consumption.

[3] Changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

3.1.2.3 Exposure from Drinking Water

Phenmedipham and its major degradate, N-(3-hydroxyphenyl)-methylcarbamate (MHPC), were considered of equal toxicity and added together for the drinking water exposure assessment. The estimated maximum (peak) surface water concentrations of phenmedipham and MHPC were 29.1 and 5.3 ppm, respectively, and the estimated chronic (average) surface water concentrations of phenmedipham and MHPC were 10.8 and 1.7 ppm, respectively, based on Tier I modelling using the screening-level computer model FQPA Index Reservoir Screening Tool (FIRST). The estimated groundwater concentrations of phenmedipham and MHPC were 0.06 and 0.07 ppm, respectively, based on Tier I modelling using the screening-level computer model Screening Concentration In Ground Water (SCIGROW). Surface water and groundwater concentrations were modelled based on the use on sugarbeets, with a seasonal application rate of 1.12 kg a.i./ha, and a default percent cropped area (PCA) of 0.87 for the surface water modelling.

The PMRA reviewed existing Canadian water monitoring data on file at the time of the re-evaluation (see Appendix III). Only one study was found in which phenmedipham was analyzed. In this study, phenmedipham was not detected in any of the samples analyzed (limit of detection: 0.02 µg/L).

3.1.2.4 Aggregate Risk Assessment

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

No acute end-point of concern was identified by the USEPA and phenmedipham was classified as “not likely to be a carcinogen to humans.” There were also no residential uses expected to contribute to short- and intermediate-term exposures for this chemical, based on its current use patterns. Consequently, aggregate risk estimates were based exclusively on chronic exposure to phenmedipham through the consumption of food and water.

A Tier I chronic aggregate risk assessment due to food and drinking water was conducted using Dietary Exposure Evaluation Model (DEEM-FCID^{TM}), which uses food consumption data from the United States Department of Agriculture’s Continuing Surveys of Food Intakes by Individuals from 1994–1996 and 1998. An estimated drinking water concentration of 12.5 ppm (for surface water) for phenmedipham plus MHPC was used in the assessment (see Section 3.1.2.3). Chronic aggregate risk was estimated to be < 1% of the cPAD for the United States population and all population subgroups, including infants and children. The USEPA considered the estimated aggregate exposure to phenmedipham to be below its level of concern, and no mitigation measures with respect to aggregate risk were required.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment and the USEPA assessment was based on conservative assumptions (i.e. residues estimated at tolerance levels, 100% of crop treated and estimate for drinking water concentration based on Tier I modelling). Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of phenmedipham in Canada, and no mitigation measures with respect to aggregate risk are required by the PMRA.

3.1.3 Cumulative Effects

The USEPA has no information indicating that phenmedipham shares a common mechanism of toxicity with desmedipham or any other substances. The USEPA also indicated in a 2005 RED, that although phenmedipham is a carbamate, it is not a cholinesterase inhibitor. Therefore, it was assumed that phenmedipham does not share a common mechanism of toxicity with other substances and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

In the 2005 RED, the USEPA concluded that the environmental fate of phenmedipham in soil varies based on the site-specific properties of the soil to which it is applied. Phenmedipham was found to be unstable in neutral and alkaline environments, but more stable under acidic conditions. Based on a laboratory aerobic soil half-life of 20 days and a half-life ranging from 13 to 136 days based on field dissipation studies, phenmedipham and its major degradate, MHPC, show low to moderate persistence under most environmental scenarios. However, under acidic conditions, the degradation rates are considerably slower and phenmedipham may persist longer. Phenmedipham was not expected to leach based on low mobility in soil, but MHPC, shows greater potential for mobility. Photo-degradation and volatilization were not expected to be important fate processes.

In water, phenmedipham was expected to adsorb to suspended solids and sediment. Laboratory studies showed that hydrolysis half-lives of phenmedipham were 14 hours and 10 minutes at pH 7 and 9 respectively, and in laboratory this chemical was stable to hydrolysis in an acidic environment (pH 5). Phenmedipham was found to photo-degrade in water, but it was expected that this would only be an important pathway in shallow and clear water bodies. Phenmedipham was found to bioaccumulate moderately in bluegill sunfish, however depuration was rapid.

No additional data or label statements were required by the USEPA to specifically address environmental fate.

To assess the ecological risk of phenmedipham to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs).

Risk assessments for marine/estuarine fish and invertebrates were not performed based on the low level of phenmedipham used along the coastal regions in the United States. As a result, the potential for phenmedipham to have adverse effects on marine/estuarine fish and invertebrates was expected to be negligible. A risk assessment for insects was also not performed because phenmedipham was found to be practically non-toxic to honey bees. As a result, the potential for phenmedipham to have adverse effects on pollinators and other beneficial insects was expected to be low.

EECs for mammals and birds were calculated using the Terrestrial Residue Exposure (T-REX) and ELL-FATE models, and were based on typical food consumption parameters by various species following applications ranging from 0.09 kg a.i./ha (six applications per year) to 1.09 kg a.i./ha of phenmedipham (one application per year). Chronic RQs did not exceed LOCs for birds. Chronic RQs did not exceed LOCs for mammals. Acute end-points of concern were not identified by the USEPA for birds and mammals, and therefore, acute risk for was not assessed.

Terrestrial plant EECs were calculated based on application rates ranging from 0.27 kg a.i./ha to 1.09 kg a.i./ha, using the Tier I model TERRPLANT, which estimates phenmedipham residues in areas adjacent to the treated field (sheet run-off), wetland areas (channelized runoff) and from spray drift. RQs did not exceed the LOC for terrestrial and wetland/riparian plants from spray drift. Therefore, the USEPA concluded that there is no risk to non-target terrestrial and semi-aquatic plants from phenmedipham.

Aquatic EECs for phenmedipham and MHPC were estimated taking into account both spray drift and runoff, and using the Tier I aquatic model GENeric Estimated Environmental Concentration (GENEEC). The aerial application of phenmedipham at the maximum single application rate (1.09 kg a.i./ha) was assumed in the assessment. Acute RQs for freshwater fish and invertebrates did not exceed LOCs. Chronic effects on freshwater organisms from exposure to phenmedipham were not assessed by the USEPA based on phenmedipham's lack of stability in water under most conditions. Generated RQs did not exceed the LOC for algae and aquatic vascular plants.

Conclusions and resulting mitigation measures derived from the USEPA RED are considered relevant to the Canadian situation. The USEPA did not require any additional mitigation measures to address specifically the risk to the environment, therefore no additional mitigation measures risk are required by the PMRA based on the USEPA's environmental risk assessment.

The PMRA calculated terrestrial and aquatic buffer zones using the most sensitive endpoints and a model, which were more conservative than the ones used by USEPA to further minimize spray drift to non-target species during ground applications. Appendix V shows the buffer zone calculations. Appendix IV lists the proposed label amendments.

3.3 Pest Control Product Policy Considerations

3.3.1 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the reevaluation, phenmedipham was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Phenmedipham was evaluated against the following Track 1 criteria: persistence in soil ≥182 days; persistence in water ≥182 days; persistence in sediment ≥365 days; persistence in air ≥2 days; bioaccumulation log K_{ow} ≥5 or Bioconcentration Factor (BCF) ≥5000 (or Bioaccumulation Factor (BAF) ≥5000). In order for phenmedipham or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The technical product was assessed against the contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern, Part 3 Contaminants of Health or Environmental Concern.* The PMRA has reached the following conclusion.

- Phenmedipham is not bioaccumulative. The *n*-octanol–water partition coefficient (log K_{ow}) is 3.39 at pH 5.9, which is below the TSMP Track 1 cut-off criterion of ≥5.0. Phenmedipham was not found to be persistent. Aerobic soil half-life is 20 days, which is below the TSMP Track 1 criterion of 180 days. Phenmedipham does not meet all Track 1 criteria; thus, it is not a candidate for Track 1 classification.

3.3.2 Contaminants and Formulants of Health or Environmental Concern

During the review process, contaminants in the technical are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[4]. The list is used as described in the PMRA Notice of Intent NOI2005-01[5] and is based on existing policies and regulations including: DIR99-03; and

[4] *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette,* Part II, Volume 142, Number 13, pages 1611–1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

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

DIR2006-02[6], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions.

- Technical grade phenmedipham does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*.

- The regulation of formulants in registered pest control products identified in the list in the *Canada Gazette* are assessed on an ongoing basis through the PMRA formulant initiatives and Regulatory Directive DIR2006-02.

4.0 Incidence Report

Starting 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment to the PMRA within a set time frame. Incidents are classified into six major categories including effects on humans, effects on domestic animals and packaging failure. Incidents are further classified by severity, in the case of humans for instance, minor effects such as skin rash, headaches, etc., to major effects such as reproductive or developmental effects, life-threatening conditions or death.

The PMRA examines incident reports and where there are reasonable grounds to suggest that the health and environmental risks of the pesticide are no longer acceptable, appropriate measures are taken. These measures can range from minor label changes to discontinuation of the product.

There were no incident reports submitted for phenmedipham as of 8 December 2008.

5.0 Organisation for Economic Co-operation and Development Status of Phenmedipham

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the current available information on the status of phenmedipham in other Organisation for Economic Co-operation and Development member countries, it appears to have been assessed by the World Health Organization's (WHO), and the technical grade active ingredient (TGAI) has been classified as a class U pesticide ("unlikely to present acute hazard in normal use") on the World Health Organization's Recommended Classification of Pesticide by Hazard and Guidelines to Classification 2000–2002 (WHO/PCS/01.5). Phenmedipham has also been reviewed by the European Commission in 2004 and approved for inclusion in the Annex I of

[6] DIR2006-02, PMRA Formulants Policy

Directive 91/414/EEC, which lists the active ingredients authorized for use as plant protection products in the European Union (2004).

As described earlier in this document, the United States, also an Organisation for Economic Co-operation and Development member, assessed the registration of all uses of phenmedipham in 2005 and concluded using phenmedipham as a pesticide does not result in unreasonable adverse effects to human health or the environment provided the risk-reduction measures recommended in the RED document were implemented.

An assessment of occupational risk was conducted in the 2005 RED and the USEPA concluded that occupational exposure was not of concern with the implementation of mitigation measures. Occupational post-application risk to agricultural workers also assessed and the USEPA concluded that post-occupational exposure was not of concern with an REI of 12 hours after application. The USEPA also assessed the carcinogenic potential of phenmedipham in the RED and the active ingredient was classified as a Group E carcinogen (no evidence of carcinogenicity). An assessment of health risk from potential exposure from food was conducted using screening level assumptions. This exposure was combined with other potential exposure from drinking water. Based on this, the United States concluded that aggregate exposure was not of concern. This evaluation also included an environmental risk assessment. Phenmedipham and its main degradate, MHPC, showed low to moderate persistence under most environmental scenarios. Phenmedipham was not expected to leach based on low mobility in soil, but MHPC, shows greater potential for mobility. However, based on the environmental risk assessment, the USEPA concluded that environmental exposure was not of concern.

The Canadian re-evaluation of phenmedipham is largely based on the USEPA's assessments and includes additional assessments. As described in Sections 3.1.1, 3.1.2 and 3.2.1 above, the PMRA has found the USEPA's environmental and human health risk conclusions to be relevant to the use of phenmedipham in Canada and requires measures to minimize spray drift to non-target species (i.e. buffer zones).

6.0 Proposed Re-evaluation Decision

The PMRA has determined that phenmedipham is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect the environment. The labels of Canadian end-use product must be amended to include the label statements listed in Appendix IV. A submission to implement label revisions will be required within 90 days of finalization of the Re-evaluation Decision. No additional data are being requested at this time.

Phenmedipham end-use products that contain more than one active ingredient under re-evaluation will be eligible for continued registration only when all of those other active ingredients are determined to be eligible.

7.0 Supporting Documentation

The PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at healthcanada.gc.ca/pmra. The PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal Toxic Substances Management Policy (TSMP) available through Environment Canada's website.

The USEPA RED document for phenmedipham available on the USEPA Pesticide Registration Status page.

The WHO's Recommended Classification of Pesticide by Hazard and Guidelines to Classification 2000–2002 documents.

The European Commission's Review Report for the active substance phenmedipham and the Annex I of Directive 91/414/EEC.

List of Abbreviations

µg	microgram
ADI	acceptable daily intake
a.i.	active ingredient
aPAD	acute population adjusted dose
bw	body weight
CAS	Chemical Abstracts Service
cPAD	chronic population adjusted dose
DACO	data code
DEEM	Dietary Exposure Evaluation Model
DWLOC	drinking water level of comparison
EDWC	estimated drinking water concentration
EEC	expected environmental concentration [also estimated environmental concentration]
FIRST	FQPA Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
ha	hectare
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LOAEL	lowest observed adverse effect level
LOC	level of concern
LOD	limit of detection
m	metre(s)
mg	milligram(s)
MHPC	N-(3-hydroxyphenyl)-methylcarbamate
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
p*K*a	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
REI	restricted-entry interval
RfD	reference dose
RQ	risk quotient

SCI-GROW	Screening Concentration in Ground Water
TC	transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Registered Products Containing Phenmedipham as of 8 December 2008

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
19204	Technical	Bayer Cropscience Inc.	Phenmedipham Technical Herbicide	Solid	97.5%
19652	Commercial	Bayer Cropscience Inc.	Betamix Emulsifiable Concentrate Postemergence Herbicide	Emulsifiable concentrate	7.5%*
28650	Commercial	Bayer Cropscience Inc.	Betamix EC Herbicide	Emulsifiable concentrate	15.3%*

*Also contains desmedipham

Appendix II Toxicological Endpoints for Phenmedipham Health Risk Assessments[a]

Exposure Scenario (Route and Period of Exposure)	Dose (mg/kg bw/day)	Study	Target UF/SF or MOE[a]
Short-term dermal (1–30 days) Intermediate-term dermal (1–6 months)	Oral NOAEL = 24 mg/kg/day (Dermal absorption rate = 10%)	Combined chronic toxicity/cancer study–rats (LOAEL=118 and 171 mg/kg/day in males and females, respectively, based on hemolytic anemia in both sexes, decreased body weight/body weight gain and food efficiency in females, increased renal pelvic epithelial hyperplasia and mineralization in males)	MOE = 100[c]
Short-term inhalation (1–30 days) Intermediate-term inhalation (1–6 months)	Oral NOAEL = 24 mg/kg/day (Inhalation absorption rate = 100%)		MOE = 100[c]
Chronic dietary (All populations)	NOAEL = 24 mg/kg/day Chronic RfD = 0.24 mg/kg/day		UF = 100[c] FQPA SF = 1 cPAD = 0.24 mg/kg/day
Acute dietary (All Population Subgroups)	None	No appropriate endpoint from oral toxicity studies	Not applicable
Incidental oral (All Durations)	Not applicable. No residential uses are registered for phenmedipham.(NOAEL of 24 mg/kg/day, if needed in future)		
Carcinogenicity	Classification: “Group E” – “Not likely to be carcinogenic to humans”		

[a] From the USEPA RED (2005)

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

[c] 10× for interspecies extrapolation ; 10x for intraspecies variability

Appendix III Detections of Phenmedipham in Canadian Water Monitoring Studies

A search of Canadian water monitoring data for phenmedipham levels was conducted. The United States monitoring data were not included in this report because these data were considered in the USEPA RED on which the Program 1 assessment is based.

In searching the current database of Canadian water monitoring data, only one study was found in which phenmedipham was analyzed. In a study conducted by Byrtus *et al*. (2002) (PMRA 1311124), the presence and levels of intensively used pesticides on locally grown crops which had not been monitored previously, as well as new pesticides broadly used across Alberta, were determined at the scoping level. Twenty water samples from four irrigation return flows in southern Alberta were collected and analyzed for phenmedipham between June and August 1999. Phenmedipham was not detected in any of the samples analyzed. The limit of detection was 0.02 µg/L.

Appendix IV Label Amendments for Products Containing Phenmedipham

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

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

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

I) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

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

DO NOT apply by air.

Buffer Zones:

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

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats such as:

- grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands;
- sensitive freshwater habitats such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands; and
- estuarine/marine habitats

Method of Application	Crop	Buffer Zones (Metres) Required for the Protection of:		
		Aquatic Habitat of Depths:		Terrestrial Habitat
		Less than 1 m	Greater than 1 m	
Field Sprayer	Sugar Beet	1 m	0 m	1 m

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.

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

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

Appendix V Inputs to Buffer Zone Models

Ground Use Data (From Canadian Labels)				
Crop	**Formulation Type**	**Method of Application**	**Number of Application**	**Maximum Application Rate (g a.i./ha)**
Sugarbeet (single application)	Emulsifiable concentrate	Field (medium)	1	726.8
Sugarbeet (repeated applications)	Emulsifiable concentrate	Field (medium)	2	726.8 (first application) 535.3 (second application)
Sugarbeet (split application ; min. application interval = 5–7 days)	Emulsifiable concentrate	Field (medium)	2	267.8
Sugarbeet (split applications ; min. application interval > 7 days)	Emulsifiable concentrate	Field (medium)	2	267.8 (first application) 726.8 (second application)

Model Input Data for Aquatic Buffer Zones (From 2005 RED)		
Half-life for aquatic buffer zones	Stable	
Most sensitive freshwater species	*Selenastrum capricornutum*	NOEC = 0.03 mg/L
Most sensitive estuarine/marine species	*Selenastrum capricornutum*	NOEC = 0.03 mg/L

Model Input Data for Terrestrial Buffer Zones (From 2005 RED)		
Half-life for terrestrial buffer zones		$t_{1/2}$ = 120 d
Most sensitive terrestrial plant species	Carrot	190 g/ha

References

Studies considered in the Chemistry Assessment

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number 1635241
Reference 1996, Technical Chemistry file PMP-BCJ-2 AE B038584, Phenmedipham, Analytical Profile of Typical Production Batches and Batch Data., PA95/116, DACO: 2.13.1, 2.13.3

Studies considered in the Environmental Risk Assessment

B. ADDITIONAL INFORMATION CONSIDERED

Published Information

PMRA Document Number 1311124
Reference Byrtus, G. *et al*., 2002. Alberta Environment; The Water Research User Group, Determination of new pesticides in Alberta's surface water (1999–2000), DACO: 8.6.