PRVD2009-06

Proposed Re-evaluation Decision

Desmedipham

(publié aussi en français)

8 April 2009

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

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Canada

HC Pub : 8164

ISBN: 978-1-100-12198-7 (978-1-100-12199-4)
Catalogue number: H113-27/2009-6E (H113-27/2009-6E-PDF)

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide desmedipham, 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 desmedipham in Canada.

An evaluation of available scientific information found that products containing desmedipham 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 desmedipham uses, new risk-reduction measures must be included on the labels of all products. No additional data are being requested at this time.

Desmedipham 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 also determined to be eligible.

This proposal affects all end-use products containing desmedipham 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 desmedipham 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 desmedipham.

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

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

The PMRA's pesticide re-evaluation program considers the 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.

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

Desmedipham, 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 the 1996 RED and the 2005 Tolerance Reassessment Eligibility Decision (TRED), the USEPA concluded that desmedipham was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American 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 section of this consultation document.

What Is Desmedipham?

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

Health Considerations

Can Approved Uses of Desmedipham Affect Human Health?

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

People could be exposed to desmedipham by consuming food and water, working as a mixer/loader/applicator or 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 group (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 desmedipham was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent 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.

Desmedipham is currently registered in Canada for use on sugar beets and could be used in other countries on crops that are imported into Canada. No specific MRLs have been established for desmedipham 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 Desmedipham Is Introduced Into the Environment?

Desmedipham 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 desmedipham 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 desmedipham 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 desmedipham to protect aquatic organisms and terrestrial plants from spray drift.

Measures to Minimize Risk

The labels of registered pesticide products include specific instructions for use. The 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 desmedipham, the PMRA is proposing further risk-reduction measures on all product labels.

Environment

- Additional advisory label statements regarding desmedipham's potential toxicity to birds
- Buffer zones to protect non-target, sensitive aquatic and terrestrial habitats

Next Steps

Before making a final re-evaluation decision on desmedipham, 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 the 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

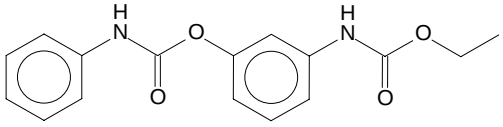
Desmedipham is a selective systemic herbicide absorbed through the leaves, with translocation primarily in the apoplast, that acts by inhibiting photosynthetic electron transport at the photosystem II receptor site.

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

The PMRA used recent assessments of desmedipham from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for desmedipham, dated 1996, and the USEPA Tolerance Reassessment Eligibility Decision (TRED) (USEPA 2005), as well as other information on the regulatory status of desmedipham in the United States, can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Desmedipham
Function	Herbicide
Chemical family	Carbamates
Chemical name	
1 International Union of Pure and Applied Chemistry (IUPAC)	Ethyl 3-phenylcarbamoyloxy-carbanilate
2 Chemical Abstracts Service (CAS)	Ethyl [3-[[(phenylamino)carbonyl]oxy]phenyl]carbamate
CAS Registry Number	13684-56-5
Molecular formula	$C_{16}H_{16}N_2O_4$
Structural formula	
Molecular weight	300.3 amu

Purity of the technical grade active ingredient	98.8% NS
Registration Number	22315

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

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure	$\leq 1 \times 10^{-6}$ mm Hg
UV–visible spectrum	No absorption between 290–750 nm
Solubility in water	1–10 ppm
n-Octanol–water partition coefficient	Log $K_{ow} \geq 3$
Dissociation constant	Not applicable, no dissociable moiety

2.3 Comparison of Use Patterns in Canada and the United States

Desmedipham is a selective systemic herbicide registered in Canada for use on sugar beets to control broad-leaved weeds. It is applied after the emergence of weeds (postemergence), and acts by inhibiting photosynthetic electron transport at the photosystem II receptor site.

The end-use products containing desmedipham registered in Canada are co-formulated with phenmedipham as emulsifiable concentrates. Desmedipham 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 7 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 interval of 5 to 7 days between the two applications.

The American and Canadian use patterns were compared. Based on the comparison of formulation types, use sites, guarantees, application methods and application rates for

desmedipham 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 sugar beets) are among those registered in the United States. Other uses of desmedipham that are registered in the United States but not in Canada include garden and table beets and Swiss chard for seed production.

- The maximum Canadian application rate (0.73 kg a.i./ha) is encompassed by the rates assessed in the RED (1.41 kg a.i./ha per application). The maximum Canadian seasonal application rate (1.26 kg a.i./ha/season) is also encompassed by the one assessed in the RED (2.19 kg a.i./ha/season).

Based on this comparison of use patterns, it was concluded that the USEPA RED and TRED for desmedipham are an adequate basis for the re-evaluation of uses of desmedipham in Canada.

All current uses are being supported by the registrant and were, therefore, considered in the re-evaluation of desmedipham. Appendix I lists all desmedipham products that are registered as of 5 December 2008 under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 1996 RED, the USEPA concluded that the use of products containing desmedipham registered at the time of publication would not pose unreasonable risks or adverse effects to humans or the environment; therefore, these products were deemed eligible for reregistration. After the RED, the USEPA published a TRED in 2005 that includes an aggregate risk assessment that meets the *Food Quality Protection Act* requirements.

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 effects observed in animals are relevant to humans and humans are more sensitive to the effects of a chemical than the most sensitive animal species.

In Canada, exposure to desmedipham may occur by consuming 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).

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.

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

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

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

The USEPA did not identify a long-term, occupational dermal or inhalation endpoint of concern. Therefore, they did not assess the occupational risk for these routes of exposure.

Seven exposure scenarios for mixers, loaders, applicators and other handlers were identified. Among the scenarios assessed in the RED, the following two exposure scenarios were considered relevant to the Canadian situation:

- mixer/loader exposure for mixing liquid groundboom treatment application
- applicator exposure for groundboom tractor equipment

Handler exposure analyses were performed using the Pesticide Handlers Exposure Database (PHED), assuming baseline personal protective equipment (PPE) (long-sleeved shirt, long pants, shoes and socks) and baseline PPE plus chemical-resistant gloves for mixing/loading. Short- (1 to 7 days) and intermediate-term (1 week to 3 months) exposure estimates assumed a maximum application rate of 1.41 kg a.i./ha, an 8-hour work day and a daily treated area of 80 acres (≈32 ha/day). Short-term risk assessments were based on a no observed effect level (NOEL) of 150 mg a.i./kg bw/day from a developmental toxicity study in the rat and intermediate-term risk assessments were based on a NOEL of 4 mg a.i./kg bw/day from a multigeneration reproduction study in the rat, both using a 5.4% dermal absorption rate.

The USEPA reported acceptable short- and intermediate-term dermal and total (dermal + inhalation) MOEs (target MOE = 100) for all occupational exposure scenarios, ranging from 566 to 166 667. Overall, the USEPA required that handlers wear chemical-resistant gloves in addition to baseline PPE. Additional label statements for good hygiene practices were also required.

The RED adequately addressed exposure scenarios associated with the uses of products containing desmedipham in Canada, and conclusions derived from the RED apply to the Canadian situation. The labels of end-use products containing desmedipham in Canada currently require baseline PPE for mixing, loading, application, clean-up and repair, and chemical-

resistant gloves for mixing and loading. The end-use product labels also include advisory statements on good hygiene practices. Therefore, no additional mitigation measures are required by the PMRA to further protect handlers.

3.1.1.2 Post-application Exposure and Risk

The USEPA noted that the toxicology endpoint of most concern for postapplication exposure was an intermediate-term (1 week to 3 months) endpoint and that the current desmedipham registration is for early-season use on sugar beets. They concluded that early season use should present minimal risk because foliar contact would be low, given the foliage area would be small at that time. Consequently, the USEPA did not assess occupational postapplication risks to agricultural workers because they determined postapplication exposure does not pose significant health risks to handlers. In lieu of a postapplication risk assessment, a restricted-entry interval of 24 hours for all desmedipham agricultural use products was required as per the American Worker Protection Standard.

These conclusions were considered applicable to the Canadian situation. Canadian labels currently require a 24-hour restricted-entry interval; Therefore, no additional mitigation measures are required by the PMRA to further protect workers from postapplication 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 a residential risk assessment was not conducted.

3.1.2.2 Exposure From Food

Desmedipham was classified by the USEPA as a Group E pesticide (evidence of non-carcinogenicity for humans). On this basis, a cancer risk assessment was not conducted.

Acute dietary risk is calculated considering the highest ingestion of desmedipham that would be likely on any one day and using food consumption and food residue values. A statistical analysis allows all possible combinations of consumption and residue levels to be combined to estimate a distribution of the amount of desmedipham residue that might be consumed in a day. A value representing the high end (95^{th} percentile) of this distribution is compared to the acute reference dose (ARfD), which is the dose to which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, the acute dietary exposure is considered acceptable. The acute reference dose is referred to as the ARfD in Canada; it is expressed as the acute population adjusted dose (aPAD) in the TRED.

Chronic dietary risk is estimated by determining how much of a pesticide's residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake (ADI), which is the dose to 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 ADI in

Canada and is expressed as the chronic population adjusted dose (cPAD) in the RED. The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix II).

Unrefined acute and chronic dietary (food) risk assessments were conducted using the Lifeline™ Model, 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. The 95th percentile acute dietary (food) exposure estimates resulted in <1% of the aPAD for the general American population and all population subgroups, including infants and children. Chronic dietary (food) exposure estimates resulted in <1% of the cPAD for the general American population and all population subgroups, including infants and children. The acute and chronic risk assessments assumed that 100% of each commodity was treated and that all residues were at tolerance levels.

The USEPA considered the estimated acute and chronic exposures to desmedipham from food to be below the level of concern, and no measures to mitigate risk from exposure through food consumption were required.

The registered uses in Canada were included in the USEPA risk assessment, and the Canadian maximum application rates are encompassed by those of the United States. Therefore, the USEPA's assessment and conclusions are considered applicable to the Canadian situation. No further measures to mitigate risk from exposure through food consumption are required by the PMRA.

3.1.2.3 Exposure From Water

Desmedipham and its major degradate, ethyl-(3-hydroxyphenyl) carbamate (EHPC), were considered of equal toxicity and added together for the drinking water exposure assessment. Tier I Estimated Drinking Water Concentrations (EDWCs) for combined residues of desmedipham plus EHPC were generated using the FQPA Index Reservoir Screening Tool (FIRST) (surface water) and Screening Concentration In GROund Water (SCIGROW) (ground water) drinking water models. Modelled EDWCs for peak and average concentrations of desmedipham plus EHPC in surface water were 130 μg/L (ppb) and 71 μg/L (ppb), respectively, and the modelled peak and average EDWCs for groundwater were both 0.039 μg/L (ppb). Surface water and groundwater drinking water concentrations were modelled based on the highest American labelled use rate (2.19 kg a.i./ha), and a default percent cropped area of 0.87. The PMRA reviewed the existing Canadian water monitoring data on file at the time of the re-evaluation (see Appendix III). Only one study was found in which desmedipham was analyzed. In this study, desmedipham 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 desmedipham (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 residential uses were expected to contribute to aggregate exposure for this chemical based on its current use pattern. Therefore, aggregate risk estimates were based on exposure from food and water only. A cancer aggregate risk assessment was not conducted based on the fact that desmedipham was classified as "not likely to be a carcinogen to humans."

In the TRED, aggregate risk was addressed by calculating acute and chronic drinking water levels of concern (DWLOCs). The DWLOC is the highest concentration of a pesticide in drinking water that would be acceptable considering the estimated exposure to that pesticide from other sources (i.e. food and residential uses). The DWLOCs were estimated using water quality models that used conservative assumptions regarding the pesticide transport from the point of application to surface and ground water. The estimated DWLOCs for the most highly exposed population, children 3–5 years old, ranged from 399 μg/L for chronic exposures to 998 μg/L for acute exposures. The DWLOCs were then compared with model-based estimates of drinking water contamination by desmedipham. Because the EDWCs (see Section 3.1.2.3) were below the DWLOCs, the USEPA concluded that residues of desmedipham in drinking water would not likely result in an acute or chronic dietary risk above the Agency's level of concern, including for infants and children, the most sensitive subgroup.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA's aggregate risk assessment. Therefore, the USEPA's aggregate exposure conclusions are considered applicable to the uses of desmedipham in Canada.

3.1.3 Cumulative Effects

The USEPA has determined that desmedipham does not have a common mechanism of toxicity with the other N-methyl carbamate pesticides. The USEPA has not made a common mechanism of toxicity finding as to desmedipham and any other substances, and desmedipham does not appear to produce a toxic metabolite produced by other substances. Therefore, it was assumed that desmedipham 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

The USEPA concluded in the 1996 RED that desmedipham is not persistent in the environment. Based on a low mobility and a tendency to bind strongly to soil organic matter, desmedipham was determined to have a low potential to leach to groundwater in most types of soil.

Desmedipham may reach surface water via spray drift and suspended particles in runoff into which desmedipham is adsorbed. Desmedipham was seen to bioaccumulate to a small extent in bluegill sunfish. However, based on depuration of >90% in 7 days, the USEPA concluded that desmedipham should not bioaccumulate significantly.

Based on this, the USEPA required additional spray drift advisory statements only on the labels of end-use products that can be applied aerially. In Canada, desmedipham end-use products are not registered for aerial application.

To assess the ecological risk of desmedipham 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 the corresponding levels of concern (LOCs).

Risk assessments for insects as well as estuarine and marine animals were not performed. Desmedipham was found to be practically non-toxic to honeybees on an acute contact basis and sugar beet is not a crop that is normally associated with high exposure to bees. Desmedipham is also not generally used in areas associated with marine and estuarine habitats. As a result, the potential for desmedipham to have adverse effects on insects and estuarine and marine animals was expected to be negligible.

EECs in food items for birds were estimated based on two applications at a rate of 1.10 kg a.i./ha (7 days apart). Acute RQs did not exceed the LOC of 1 for birds feeding on short grass, tall grass, broad-leaved plants, insects, fruits and pods. Chronic RQs exceeded the LOC for birds feeding on tall grass, broad-leaved plants and short grass, respectively.

EECs in food items for mammals were estimated based on a single application at a rate of 1.41 kg a.i./ha and two applications at a rate of 1.10 kg a.i./ha (7 days apart). Acute RQs did not exceed the LOC of 1 for mammals feeding on short grass, tall grass and broad-leaved plants. For chronic risk, the expected residues of desmedipham in plants were greater than a no observed effect level (NOEL) based on minor blood effects. However, the USEPA indicated in the RED that the changes in the blood observed in this study may or may not have ecological significance to the survival and reproduction of wild mammals.

Exposure to non-target terrestrial and semi-aquatic plants was estimated based on pesticide loading from runoff and spray drift. Exposure from runoff differs between plant types; terrestrial plants are assumed to be subject to sheet runoff, whereas semi-aquatic plants are assumed to be subject to channelized runoff. Exposure estimates were based on a single application at a rate of 1.41 kg a.i./ha. RQs did not exceed the LOC of 1 from a combination of runoff and spray drift. However, risks resulting from exposure to spray drift on foliage could not be quantitatively assessed because data from typical end-use product studies were not available. Since desmedipham is used to control emerged weeds, the USEPA concluded that exposure to desmedipham from spray drift may pose some risk to non-target terrestrial and semi-aquatic endangered or non-endangered plants. Confirmatory data was requested by the USEPA (i.e. seedling emergence and vegetative vigour testing with a typical end-use product).

Aquatic EECs were estimated taking into account both spray drift and runoff, using the GENeric Expected Environmental Concentration Program (GENEEC). One application of 1.41 kg a.i./ha or two applications per year at an application rate of 1.10 kg a.i./ha (7 days apart) were assumed in the calculations. Acute RQs for freshwater fish and invertebrates did not exceed the LOC of 1 at application rates of 1.41 kg a.i./ha (one application) and 1.10 kg a.i./ha (two applications). Based on this data, the USEPA concluded that desmedipham should have little or no acute effects on freshwater fish and invertebrates. Due to the relatively low acute toxicity and low persistence in water of desmedipham, a chronic risk assessment for freshwater fish and invertebrates was not conducted. Generated RQs for algae and aquatic vascular plants did not exceed the LOC of 1 at an application rate of 1.10 kg a.i./ha (two applications). The USEPA concluded that concentrations of desmedipham in water are expected to have minimal effects on non-target endangered or non-endangered aquatic plants. However, as with terrestrial plants, the drift of a typical end-use product may have adverse effects on aquatic plants with foliage above the water. Confirmatory data was requested by the USEPA (i.e. seedling emergence and vegetative vigour testing with a typical end-use product).

Due to data gaps and/or concerns regarding acute and/or chronic risks to birds and non-target plants (terrestrial, semi-aquatic and aquatic), the USEPA required spray drift advisory label statements for end-use products that can be applied aerially.

The American use pattern for desmedipham encompasses the Canadian use pattern; thus, the USEPA's risk-reduction measures should be applied to Canadian products containing desmedipham. In Canada, however, desmedipham end-use products are not registered for aerial application; therefore, the USEPA requirement for spray drift advisory label statements does not apply to the Canadian situation.

Based on PMRA general practices, a label statement warning about the potential toxicity to birds should be required on all end-use products. To further minimize spray drift to non-target species during ground applications, the PMRA also calculated terrestrial and aquatic buffer zones using the most sensitive endpoints and a model that is more conservative than those used by the USEPA. Appendix IV shows the required label amendments and Appendix V the buffer zone calculations.

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 (TSMP), 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 re-evaluation, desmedipham 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*. Desmedipham 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 ≥5000 (or bioaccumulation factor ≥5000). In order for desmedipham 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 conclusions.

> Desmedipham does not meet Track 1 criteria. Desmedipham does not meet the Track 1 criterion for persistence, as its half-life value in soil (7.7 days) is below the Track 1 criterion. Desmedipham also does not meet the Track 1 criterion for persistence in air because volatilisation is not an important route of dissipation and long-range atmospheric transport is unlikely to occur based on its vapour pressure (3×10^{-9} Torr) and Henry's law constant (estimated to be 1.69×10^{-10} atm-m^3 mol^{-1}). Desmedipham does not meet the Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (log K_{ow} 3.39 at pH 5.9) and BCF (≤ 159×) are below the Track 1 criterion. Therefore, desmedipham does not meet all the Track 1 criteria and is not considered a Track 1 substance.

3.3.2 Contaminants and Formulants of Health or Environmental Concern

During the review process, contaminants in the technical product are compared against the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern maintained in the *Canada Gazette*. [1] The list is used as described in the PMRA Notice of Intent NOI2005-01[2] and is based on existing policies and regulations including Regulatory Directives DIR99-03 and DIR2006-02[3]. The list also takes 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 desmedipham does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*.

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1 *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.

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

3 DIR2006-02, *PMRA Formulants Policy*; DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy.*

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

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

The PMRA 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, ranging from minor label changes to discontinuation of the product.

No incident reports were submitted for desmedipham as of 5 December 2008.

5.0 OECD Status of Desmedipham

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 desmedipham in other OECD member countries, the technical grade active ingredient has been classified as a class U pesticide (i.e. “unlikely to present acute hazard in normal use”) on the World Health Organization’s (WHO) Recommended Classification of Pesticide by Hazard and Guidelines to Classification 2000-2002 (WHO/PCS/01.5). The European Commission also reviewed desmedipham in 2004 and approved it for inclusion in Annex I of Directive 91/414/EEC, which lists the active ingredients authorized for use as plant protection products in the European Union (EC, 2004).

As described earlier in this document, the United States, also an OECD member, assessed the registration of all uses of desmedipham in 1996 and concluded that using desmedipham 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. The USEPA also assessed the aggregate health risk from uses of desmedipham and published the results in a Tolerance Reassessment Eligibility Decision (TRED) document in 2005.

The USEPA conducted an assessment of occupational risk and concluded in the 1996 RED that occupational exposure was not of concern with the implementation of mitigation measures.

Occupational postapplication risk to agricultural workers was not assessed because the USEPA determined that health risks to handlers from postapplication do not pose a significant risk. The USEPA also assessed the carcinogenic potential of desmedipham in the RED and the active ingredient was classified as a Group E carcinogen (no evidence of carcinogenicity). An assessment of the health risk from potential exposure from food was conducted in the 2005 TRED using screening level assumptions, including tolerance level residues. 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. The USEPA RED also included an environmental risk assessment. The USEPA found that desmedipham was not persistent and had low potential to leach to groundwater in most soil, based on low mobility and a tendency to bind strongly to soil organic matter. Based on the environmental risk assessment, the USEPA concluded that environmental exposure was not of concern with the implementation of mitigation measures.

As indicated above, the Canadian re-evaluation of desmedipham is largely based on the USEPA's 1996 and 2005 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 desmedipham in Canada and proposes the requirement of buffer zones to minimize spray drift to non-target species.

6.0 Proposed Re-evaluation Decision

The PMRA has determined that desmedipham is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use products 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 the finalization of the re-evaluation decision. No additional data are being requested at this time.

Desmedipham 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

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.hc-sc.gc.ca/cps-spc/pest/index-eng.php. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.
The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for desmedipham is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

The WHO's Recommended Classification of Pesticide by Hazard and Guidelines to Classification 2000-2002 documents are available at http://whqlibdoc.who.int/hq/2002/a76526.pdf.

The European Commission's Review report for the active substance desmedipham is available at http://ec.europa.eu/food/plant/protection/evaluation/exist_subs_rep_en.htm and the Annex I of Directive 91/414/EEC is available at www.pesticides.gov.uk/approvals.asp?id=623.

List of Abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
aPAD	acute population adjusted dose
ARD	acute reference dose
ARfD	acute reference dose
bw	body weight
CAS	Chemical Abstracts Service
cPAD	chronic population adjusted dose
DACO	data code
DWLOC	drinking water level of comparison
EC_{50}	effective concentration on 50% of the population
EDWC	estimated drinking water concentration
EEC	expected environmental concentration
EHPC	ethyl-(3-hydroxyphenyl) carbamate
FIRST	*Food Quality Protection Act* Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
GENEEC	GENeric Expected Environmental Concentration Program
ha	hectare(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LOC	level of concern
LOEL	lowest observed effect level
mg	milligram(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NS	nominal by specification
OECD	Organisation for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
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
SCIGROW	Screening Concentration In GROund Water
TRED	Tolerance Reassessment Eligibility Decision
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UF/SF	uncertainty and/or safety factors
UV	ultraviolet

Appendix I Registered Products Containing Desmedipham as of 5 December 2008

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
22315	Technical	Bayer Cropscience Inc.	Desmedipham Technical Herbicide	Solid	98.8%
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 phenmedipham.

Appendix II Toxicological Endpoints for Desmedipham Health Risk Assessments

Exposure Scenario	Dose (mg/kg bw/day)	Study (Toxicological Effects)	UF/SF or MOE[a]
Short-term dermal and inhalation (1 to 7 days)[b]	NOEL = 150 Dermal absorption rate = 5.4%	Developmental study in the rabbit (LOEL = 450 mg/kg bw/day based on decreased body weight)	MOE = 100[d]
Intermediate-term dermal and inhalation (1 week to 3 months)[b]	NOEL = 4	Two-generation reproduction study in the rat (LOEL = 20 mg/kg bw/day based on anemia and increased spleen weight)	MOE = 100[d]
Acute dietary (all populations)[c]	Maternal NOAEL = 10 RfD = aPAD = 0.10	Developmental toxicity study in the rat (LOEL = 100 mg/kg bw/day based on increased maternal methemoglobin)	UF = 100[d] FQPA SF = 1×
Chronic dietary (all populations)[c]	NOAEL = 4 RfD = cPAD = 0.04	Two-generation reproduction study in the rat (LOEL = 20 mg/kg bw/day based on anemia and increased spleen weight)	UF = 100[d] FQPA SF = 1×
Carcinogenicity[c]	Classification: "Group E"—"not likely to be carcinogenic to humans"		

[a] 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.

[b] From USEPA RED (1996).

[c] From USEPA TRED (2005).

[d] 10× for interspecies extrapolation; 10× for intraspecies variability.

Appendix III Detections of Desmedipham in Canadian Water Monitoring Studies

A search of Canadian water monitoring data for desmedipham levels was conducted. The American 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 desmedipham was analyzed. In the study conducted by Byrtus et al. (2002) (PMRA# 1311124), the presence and levels of intensively used pesticides on locally grown crops that 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 desmedipham between June and August 1999. Desmedipham 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 Desmedipham

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 the labels of currently registered products should not be removed unless it contradicts the label statements given below.

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:				
		Freshwater Habitat of Depths:		Estuarine/Marine Habitat of Depths:		Terrestrial habitat
		Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m	
Field sprayer	Sugar beet (reduced rate applications)	1	1	0	0	1
	Sugar beet (full rate applications)	1	1	1	0	1

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**.

TOXIC to birds.

Appendix V Inputs to Buffer Zone Models

Ground Use Data (from Canadian labels)				
Crop	**Formulation Type**	**Method of Application**	**Number of Applications**	**Maximum Application Rate (g a.i./ha)**
Sugar beet (single application)	Emulsifiable concentrate	Field (medium)	1	726.8
Sugar beet (repeated applications)	Emulsifiable concentrate	Field (medium)	2	726.8 (first application) 535.3 (second application)
Sugar beet (split application; min. application interval = 5–7 days)	Emulsifiable concentrate	Field (medium)	2	267.8
Sugar beet (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 1996 RED)		
Half-life for aquatic buffer zones	Stable	
Most sensitive freshwater species	*Navicula pelliculosa*	½ EC_{50} = 0.022 mg/L
Most sensitive estuarine/marine species	*Skeletonema costatum*	½ EC_{50} = 0.15 mg/L

Model Input Data for Terrestrial Buffer Zones (from 1996 RED)		
Half-life for terrestrial buffer zones	$t_{1/2}$ = 8 days	
Most sensitive terrestrial plant species	Tomato	348 g/ha

References

Studies considered in the Chemistry Assessment

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

PMRA Document Number	Reference
1103777	2005. Desmedipham Technical Herbicide; Part 2 Product Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient (TGAI) or an Integrated System Product (ISP), 05007DC, DACO: 2.0, 2.1, 2.11, 2.11.1, 2.11.2, 2.11.3, 2.11.4, 2.12.1

Studies considered in the Environmental Risk Assessment

A. ADDITIONAL INFORMATION CONSIDERED

Published Information

PMRA Document Number	Reference
1311124	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.