PRVD2008-25

Proposed Re-evaluation Decision

Carbathiin and Oxycarboxin

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Overview

Proposed Re-evaluation Decision

After a re-evaluation of the fungicide carbathiin and oxycarboxin, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing carbathiin (as a seed treatment) and oxycarboxin (for control of rust on ornamentals grown in enclosed commercial structures) for the sale and use in Canada.

Carbathiin products registered for use as a tree seedling treatment, ornamentals outdoor and residential plantscapes treatment will no longer be supported by the registrant. Carbathiin and oxycarboxin products registered in Canada for use as a turf treatment will no longer be supported by the registrant.

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

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

This proposal affects all end-use products containing carbathiin or oxycarboxin 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 carbathiin and oxycarboxin, and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

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 carbathiin.

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).

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

What Health Canada Considers 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.

Carbathiin and oxycarboxin, two active ingredients in the current re-evaluation cycle, have 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 2004 RED documents, the USEPA concluded that carbathiin and oxycarboxin were 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 Are Carbathiin and Oxycarboxin?

Carbathiin is a systematic fungicide that is applied to seeds prior to planting to control various fungi that cause seed and seedling diseases such as smut, rot and blight. Carbathiin is applied both by commercial seed treaters and by on-farm applicators. Uses include seed treatment for barley, beans, canola, chickpeas, corn, flax, lentils, mustard, oats, onion, peas, rapeseed, rye, soybeans, triticale, wheat and bromegrass.

Oxycarboxin (carboxin sulfone), a metabolite of carbathiin, is a systematic fungicide applied as a watering solution to control rust on carnations in enclosed commercial greenhouses.

Health Considerations

Can Approved Uses of Carbathiin or Oxycarboxin Affect Human Health?

Carbathiin is unlikely to affect human health when used according to the revised label directions. Oxycarboxin is unlikely to affect your health when used according to the label directions.

Exposure to carbathiin may occur through diet (food and water), while conducting seed treatment activities or when loading and planting carbathiin-treated seed. Exposure to oxycarboxin is limited to a mixer/loader/applicator and to workers entering treated sites.

The PMRA considers two key factors, when assessing health risk: 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 carbathiin was unlikely to affect human health provided that risk-reduction measures were implemented. No mitigation measures were required in respect to oxycarboxin. These conclusions apply to the Canadian situation, and for carbathiin, equivalent risk-reduction measures are required.

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.

Carbathiin is currently registered in Canada as a seed treatment for barley, beans, canola, chickpeas, corn, flax, lentils, mustard, oats, onion, peas, rapeseed, rye, soybeans, triticale, wheat and bromegrass, and could be used in other countries on crops that are imported into Canada. No specific MRLs have been established for carbathiin 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 the 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.

Use of oxycarboxin is currently limited in Canada to non-food uses in enclosed commercial greenhouses. No MRLs have been established for oxycarboxin.

Environmental Considerations

What Happens When Carbathiin and Oxycarboxin Are Introduced Into the Environment?

Additional risk reduction measures are required on carbathiin labels. Carbathiin is unlikely to affect non-target organisms when used according to the revised label directions.

Environmental risk is assessed by the risk quotient method – the ratio of the estimated environmental concentration to the relevant effect's 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 results of chronic risk assessments indicate there is a potential for chronic risk to seed-eating birds and mammals consuming carbathiin-treated seeds.

The USEPA concluded that the reregistration of carbathiin was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Given the oxycarboxin use is limited to enclosed commercial structures, environmental exposure is not expected.

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 carbathiin, the PMRA is proposing further risk-reduction measures for product labels.

Human Health Risks

Carbathiin

- additional protective equipment to protect workers involved in seed treatment activities and in loading and planting treated seeds are required.

Oxycarboxin

No mitigation measures required.

Environmental Risks

Carbathiin

- additional advisory label statements to reduce potential surface and groundwater contamination are required.
- additional advisory label statements to protect non-target sensitive terrestrial animals are required.

Oxycarboxin

No mitigation measures are required.

Next Steps

Before making a final re-evaluation decision on carbathiin and oxycarboxin, 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] 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

Carbathiin is a fungicide that selectively concentrates in fungal cells and acts by inhibiting the mitochondrial complex II (succinate dehydrogenase) in the respiratory electron transport chain. Oxycarboxin (carboxin sulfone), a carbathiin metabolite, has been shown to block mitochondrial complex II in a similar way as carbathiin.

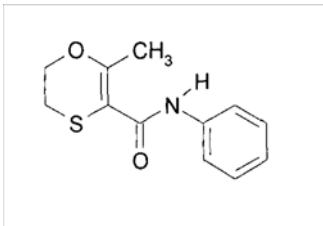
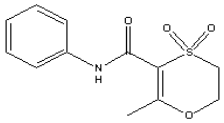
Following the re-evaluation announcement for carbathiin and oxycarboxin, the registrant of the technical grade active ingredients in Canada indicated their intention to support carbathiin use as a seed treatment (including bulbs/corms) and oxycarboxin use on a greenhouse non-food crop. Remaining uses of carbathiin on tree seedling treatment, ornamentals, outdoor and residential plantscapes are no longer supported by the registrant. Carbathiin and oxycarboxin uses as a turf treatment are no longer supported by the registrant. Therefore, seed treatment with carbathiin and greenhouse crop (carnations) treatment with oxycarboxin are the only uses being evaluated in this document.

The PMRA used recent assessments of carbathiin and oxycarboxin from the USEPA. The 2004 RED documents for carbathiin and oxycarboxin, tolerance actions published in the 2006 Federal Register as well as other information on the regulatory status of carbathiin and oxycarboxin 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	**Carbathiin**	**Oxycarboxin**
Function	Fungicide	Fungicide
Chemical Family	Carboxamide	Carboxamide
Chemical name		
1 International Union of Pure and Applied Chemistry (IUPAC)	5,6-dihydro-2-methyl-1,4-oxathi-ine-3-carboxanilide	5,6-dihydro-2-methyl-1,4-oxathi-ine-3-carboxanilide 4,4-dioxide
2 Chemistry Abstracts Service (CAS)	5,6-dihydro-2-methyl-phenyl-1,4-oxathiin-3-carboxamide	5,6-dihydro-2-methyl-phenyl-1,4-oxathiin-3-carboxamide 4,4-dioxide
CAS Registry Number	5234-68-4	5259-88-1

Molecular Formula	$C_{12}H_{13}NO_2S$	$C_{12}H_{13}NO_4S$
Structural Formula		
Molecular Weight	235.31	267.3
Pest Control Product (PCP) Number of the TGAI	18722	18114

The carbathiin technical grade active ingredient was analysed for aniline, an impurity of toxicological concern as identified in Section 2.13.4 of Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*. Aniline was not detected above the limit of detection (LOD) of 0.05%. No other impurities of toxicological concern are expected to be present in technical carbathiin.

2.2 Physical and Chemical Properties

Property	Carbathiin	Oxycarboxin
Vapour pressure at 25°C	0.020 mPa	$<5.6 \times 10^{-3}$ mPa
Henry's law constant	3.24×0^{-5} Pa m^3 mol^{-1}	$<1.07 \times 10^{-6}$ Pa m^3 mol^{-1}
UV/Visible spectrum	not expected to absorb UV at λ > 300nm (λ max ≈ 252 nm over a range of 290 to 590 nm)	Not expected to absorb UV at λ>300 nm
Solubility in water	0.147 g/L	1.4 g/L
***n*-Octanol–Water partition coefficient**	log K_{ow} = 2.3	log K_{ow} = 0.772
Dissociation constant	p*K*a < 0.5	Not available

2.3 Comparison of Use Patterns in Canada and the United States

Carbathiin

Carbathiin is a fungicide registered in Canada for use as a seed treatment to control various fungi that cause seed and seedling diseases (smut, rot and blight). Uses include seed treatment for barley, beans, canola, chickpeas, corn, flax, lentils, mustard, oats, onion, peas, rapeseed, rye, soybeans, triticale, wheat and bromegrass, as well as bulbs and corms. Carbathiin is applied as a seed treatment with maximum application rates ranging from 32 g a.i./100 kg of seed (triticale) to 750 g a.i./100 kg of seed (onion), equivalent to 32 and 126 g a.i./ha, based on planting rates for each crop. The end-use products, registered in Canada, are formulated as dust/powder, solution and suspension.

The American and Canadian use patterns were compared. Carbathiin is registered as a seed treatment for commercial and on-farm uses, in both Canada and the United States. The formulation types and application rates of Canadian products are encompassed by those eligible for reregistration in the United States. Canadian use sites are encompassed by the American use site with the exception of rapeseed, mustard, chickpeas, lentils, peas and flax. Based on this comparison of use patterns, it was concluded that the USEPA RED document on carbathiin is an adequate basis for re-evaluating the uses of carbathiin in Canada.

Only seed treatment (including bulb/corms) with carbathiin is supported by the registrant. Remaining uses of carbathiin are no longer supported, therefore, not considered in this re-evaluation document. Appendix I lists all carbathiin products that are registered as of 1 April 2008.

Oxycarboxin

Oxycarboxin is a fungicide registered in Canada for the control of rust on carnations in commercial greenhouses. The oxycarboxin end-use product is a liquid formulation and is applied as a watering solution every 10 days with the maximum application rate of 0.16 g a.i./L. Oxycarboxin is registered for greenhouse non-food crops (carnations) in both Canada and the United States.

Based on the comparison of use patterns between the United States and Canada, it was concluded that the USEPA RED document for oxycarboxin is an adequate basis for the re-evaluation of oxycarboxin use in Canada. The use of oxycarboxin as a turf treatment for control of snow mold is no longer supported by the registrant and is therefore not considered in this re-evaluation document.

3.0 Impact on Human Health and the Environment

In their 2004 RED documents, the USEPA concluded that the end-use products formulated with carbathiin and oxycarboxin 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. After the carboxin RED, the USEPA published tolerance actions in the Federal Register revoking and modifying certain tolerances for carboxin in or on raw agricultural commodities.

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 carbathiin may occur through consumption of food and water, when involved in seed treatment activities or when loading and planting carbathiin treated seeds. Exposure to oxycarboxin may occur when involved in treatment activities or when entering treated sites in greenhouses.

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).

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 a 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.

3.1.1.1 Mixer/Loader Exposure and Risk

Carbathiin
Workers can be exposed to carbathiin when involved in seed treatment activities in both on-farm and in commercial settings. Only short- and intermediate-term exposure scenarios are expected based on a label directed use pattern. The USEPA identified six occupational scenarios for carbathiin for which separate dermal and inhalation exposures were estimated. The following occupational scenarios assessed by the USEPA are relevant to the Canadian situation:

- on-farm seed treatment with dry formulation
- on-farm seed treatment with liquid formulation
- commercial loaders/applicators
- commercial baggers
- commercial sowers
- multiple commercial activities

The above mentioned relevant occupational handler scenarios, assuming long pants, a long-sleeved shirt and gloves on workers, resulted in MOEs ranging from 100 to 33 000 for dermal, and from 460 to 25 000 for inhalation exposure. Results indicated that occupational risk is below the USEPA's level of concern.

The RED adequately addressed occupational exposure scenarios associated with the uses of products containing carbathiin as a seed treatment in Canada, and conclusions derived from the RED apply to the Canadian situation.

The PMRA requires that workers wear the basic personal protective equipment (PPE) consisting of a long-sleeved shirt, long pants, socks plus shoes and chemical-resistant gloves. In addition, based on good hygiene practises and to be consistent with other seed treatment recommendations, a dust mask is required for workers involved in seeds treatment with dust/powder, and for baggers, sowers and handlers of treated seeds in commercial settings.

Oxycarboxin
Oxycarboxin was considered to be toxicologically equivalent to carbathiin, therefore, the endpoints selected for carbathiin were used by the EPA to estimate occupational exposure and risk for oxycarboxin (Appendix I, Table 1).

Workers can be exposed to oxycarboxin when mixing, loading and applying the fungicide using high pressure handwand equipment or a watering system. Only short- and intermediate-term exposure scenarios are expected for occupational scenarios based on a label directed use pattern.

The MOEs calculated for short-term exposure (mixing, loading and application) were 1000 for dermal exposure and 530 for inhalation exposure, above the USEPA's target MOE of 100.

The RED document adequately addressed potential exposure scenarios associated with the Canadian uses of oxycarboxin, and conclusions derived from the RED document are considered to be applicable to the Canadian situation. No further mitigation measures are required.

3.1.1.2 Postapplication Exposure and Risk

Carbathiin
The postapplication occupational risk assessment considered exposure of workers involved in loading and planting carbathiin treated seeds. Such activities would take place for only a few days in the spring; therefore, postapplication exposure to carbathiin-treated seeds was considered to be short-term in duration.

MOEs calculated for short-term exposure for loading and planting treated seeds (>1 000 for dermal and >1 800 for inhalation exposure) were above the USEPA's target MOE of 100, indicating that the postapplication risk is below the USEPA's level of concern.

The RED adequately addressed exposure scenarios associated with the Canadian uses of carbathiin. To further minimize exposure to carbathiin, the PMRA requires that workers involved in loading and planting carbathiin-treated seeds wear a long-sleeved shirt, long pants and chemical-resistant gloves.

Oxycarboxin
The USEPA determined that occupational postapplication exposure, such as exposure of workers who re-enter areas previously treated with oxycarboxin, is well below handlers (mixer/loader/applicator) exposures and, therefore, is not of concern.

A restricted-entry interval (REI) of 12 hours for oxycarboxin agricultural use products is required by the USEPA as per the Worker Protection Standard.

The RED adequately addressed exposure scenarios associated with the Canadian uses of carbathiin. The PMRA requires an REI of 12 hours for workers entering oxycarboxin treated sites to further minimize postapplication exposure.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Exposure From Food and Drinking Water

Carbathiin
No toxicological endpoint attributed to a single oral dose was identified. Therefore, no acute dietary risk assessment was performed by the USEPA.

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

The USEPA conducted a Tier 1 conservative dietary risk assessment assuming that residues are present at the tolerance level for all registered uses and 100% of crops are treated. The chronic exposure estimates for the whole United States population and population subgroups were below 100% of the cPAD, with the highest chronic exposure obtained for children 1 to 2 years old, taking up to 36% of the cPAD. The chronic dietary risk was below the USEPA's level of concern.

Carbathiin was found to be a mobile compound which degrades rapidly in the environment to form carboxin sulfoxide and carboxin sulfoxide. Due to rapid aerobic degradation in soil, carbathiin leaching into nearby water bodies was assumed to be unlikely, but carbathiin sulfoxide may reach the groundwater and runoff or drift into the surface water. Thus, the USEPA determined that the residue of concern in drinking water is carbathiin and its sulfoxide degradate.

Screening level models were used to estimate carbathiin concentration in the surface and ground water. The estimated drinking water concentrations (EDWCs) of carbathiin in surface water and groundwater were 0.63 µg/L and 0.95 µg/L, respectively, based on a use expected to represent the worst case scenario, i.e. peanut seeds treated with carbathiin at 0.42 kg/ha.

The USEPA's assessment encompasses Canadian registered uses of carbathiin as a seed treatment, with the exception of the use for mustard, lentils, chickpeas, peas and flax. Despite differences in use pattern between Canada and the United States, the USEPA assessment is considered applicable to the Canadian situation, because it was based on conservative Tier 1 assumptions.

Oxycarboxin
The use of oxycarboxin is limited to ornamentals in enclosed commercial greenhouses, and there is no residential use of oxycarboxin. Therefore, no dietary risk assessment was performed.

3.1.2.2 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to carbathiin (i.e. from food, water and residential exposures). The USEPA calculated drinking water levels of comparison (DWLOCs), which represent the concentration of a chemical in drinking water that would be acceptable as an upper limit in the light of total aggregate exposure to that chemical from food and water.

Drinking water concentration estimates (EDWCs) were compared to the DWLOC. The EDWCs for both surface water (0.63 µg/L) and groundwater (0.095 µg/L) were below the most conservative chronic DWLOC (26 µg/L for children 1 to 2 years old), indicating that aggregate chronic exposure to carbathiin was below the USEPA's level of concern.

The USEPA determined that aggregate risk exposure to carbathiin in food and drinking water and to oxycarboxin from plants (carnations) treated in commercial greenhouses is not of concern.

Potential Canadian aggregate exposure scenarios were adequately addressed by the RED document. The estimate of carbathiin concentration in drinking water was based on the worst case scenario (application to peanuts at 0.42 kg a.i./ha) encompassing Canadian carbathiin maximum application rates. The USEPA aggregate exposure conclusions are considered applicable to the uses of carbathiin and oxycarboxin in Canada. No additional mitigation measures are required at this time.

3.1.3 Cumulative Effects

The USEPA did not find a common mechanism of toxicity for carbathiin and other substances.

3.2 Environment

3.2.1 Environmental Risk Assessment

Carbathiin

The USEPA concluded that carbathiin is a mobile compound which transforms rapidly in the environment to form carboxin sulfoxide and carboxin sulfone (oxycarboxin), which tend to be more persistent than the parent compound. Carboxin sulfoxide may reach the groundwater and can be expected to runoff or drift into the surface water.

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

When carbathiin is exclusively used as a seed treatment, its effect on terrestrial animals is likely limited to terrestrial seed-eating birds and mammals, while the exposure to aquatic species is expected to be negligible.

The results of toxicological studies suggested that carbathiin is practically nontoxic to birds and mammals on acute exposure basis. While, chronic effects have been shown, chronic exposure is not likely given the following reasons.

- Seeds are planted about 2.5 cm deep in the soil.
- Carbathiin can diffuse out of seed coat into the soil.
- Treated seed is available for consumption for only about 10 days before it germinates and become unavailable.

Based on the potential for the possible contamination of water used for human or animal consumption, and to further protect terrestrial birds and mammals from accessing carbathiin treated seeds, the USEPA required additional advisory statements to be added to the labels.

The American use pattern encompasses the Canadian use of carbathiin as a seed treatment, and statements similar to those required by the USEPA are to be added to Canadian labels.

Oxycarboxin
The USEPA did not perform an environmental risk assessment for oxycarboxin because its use is limited to enclosed commercial greenhouses.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal 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.

The federal Toxic Substances Management Policy and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of carbathiin. The PMRA has reached the following conclusions.

- Carbathiin is not bioaccumulative, the *n*-octanol–water partition coefficient (log K_{ow}) is 2.3, which is below the TSMP Track 1 cutoff criterion of ≥ 5.0. Carbathiin was not found to be persistent, an aerobic soil half-live is 1.26 days, which is below the TSMP Track 1 criterion of 180 days. Carbathiin does not meet all Track 1 criteria; thus, it is not a candidate for Track 1 classification.

- Oxycarboxin is not bioaccumulative. The *n*-octanol–water partition coefficient (log K_{ow}) is 0.722, which is below the TSMP Track 1 cutoff criterion of ≥ 5.0. Oxycarboxin does not meet all Track 1 criteria, thus it is not a candidate for Track 1 classification.

- No TSMP Track1 substances as identified in Regulatory Directive DIR99-03, Appendix II, are expected to be present in the technical product of carbathiin.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

4.0 Proposed Re-evaluation Decision

Carbathiin, for use as a seed treatment, 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 remaining uses of carbathiin are not supported by the registrant and need to be removed from the end-use product label. The labels of Canadian end-use products must be amended to include the label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days after the re-evaluation decision. No additional data are being requested at this time.

Oxycarboxin, for control of rust on carnations in enclosed commercial greenhouses, is acceptable for continued registration. No mitigation measures are required at this time.

Carbathiin 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.

5.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and data code (DACO) tables can be found on our website at www.pmra-arla.gc.ca. 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; or e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available on Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED documents for carbathiin and oxycarboxin are available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

USEPA 2006 Federal Register. FRL-8093-5. Benzaton, Carboxin, Dipropyl Isocinchomeronate, Oil of Lemongrass (Oil of Lemon) and Oil of Orange; Tolerance Actions.

List of Abbreviations

µg	microgram
ADI	acceptable daily intake
a.i.	active ingredient
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
FIRST	FQPA Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
ha	hectare
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration to 50%
LD_{50}	lethal dose to 50%
LOC	level of concern
MOE	margin of exposure
MRL	maximum residue limit
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
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
PXT	oxycarboxin
RED	Reregistration Eligibility Decision
RQ	risk quotient
SCI-GROW	Screening Concentration in Ground Water
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet
VIT	carbathiin

Appendix I Registered Products Containing Carbathiin and Oxycarboxin as of 4 June 2008

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
10878	Commercial	Chemtura Canada Co. Cie	HRC Liquid Systematic Fungicide	Solution	PTX* 5%
10959	Commercial	Chemtura Canada Co. Cie	PRO-GRO Systematic dust seed protectant	Dust	VIT** 30%
11423	Commercial	Chemtura Canada Co. Cie	Vitaflo280 Fungicide	Suspension	VIT 15.59%
13051	Commercial	Chemtura Canada Co. Cie	Vitavax–Captan 30W systemic soil fungicide	Wettable powder	VIT 6%
13431	Commercial	Chemtura Canada Co. Cie	Arrest-75W - Systemic turf fungicide	Wettable powder	VIT 20% PTX 5%
18114	Technical	Chemtura Canada Co. Cie	Plantvax Tech	Powder	PTX 99%
18722	Technical	Chemtura Canada Co. Cie	Vitavax Tech	Powder	VIT 98%
18788	Commercial	Chemtura Canada Co. Cie	Anchor Systematic and contact seed protectant	Suspension	VIT 6.7%
21174	Commercial	Chemtura Canada Co. Cie	Vitaflo220 Systematic seed protectant	Suspension	VIT 22%
22473	Commercial	Chemtura Canada Co. Cie	Vitaflo280 Undyed seed protectant	Suspension	VIT 15.6%
23430	Commercial	Chemtura Canada Co. Cie	Crown Systematic and contact seed protectant	Solution	VIT 9%
25862	Commercial	Chemtura Canada Co. Cie	Vitavax RS Seed protectant	Suspension	VIT 5.97%
27009	Commercial	Chemtura Canada Co. Cie	Vitavax RS undyed seed protectant	Suspension	VIT 6.26%
27117	Commercial	Chemtura Canada Co. Cie	Arrest Dry - Systematic turf Fungicide	Granules	VIT 1.26% PTX 0.31%
27174	Commercial	Bayer CropScience Inc.	GAUCHO CS FL Systematic Insecticide and fungicide	Suspension	VIT 47.6 g/L
27550	Commercial	Chemtura Canada Co. Cie	Vitavax Flowable Fungicide	Suspension	VIT 20.8%
27555	Commercial	Chemtura Canada Co. Cie	Vitavax200 Flowable Fungicide	Suspension	VIT 17%

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
27564	Commercial	Bayer CropScience Inc.	Prosper FL Flowable Insecticide and Fungicide Seed Treatment	Suspension	VIT 4.4 %
27595	Commercial	Chemtura Canada Co. Cie	Vitavax Powder - Systematic Seed Protectant	Powder	VIT 26.7%
27697	Commercial	Chemtura Canada Co. Cie	Vitaflo250, Liquid Suspension Systematic Seed Protectant	Suspension	VIT 25.3%

* PXT = oxycarboxin

** VIT = carbathiin

Appendix II Toxicological Endpoints for the Carbathiin Health Risk Assessment

Exposure Scenario	Dose (mg/kg bw/day)	Study	UF/SF or MOE[a]
Acute dietary (all population subgroups)	No toxicological endpoint attributable to a single oral dose was identified in available toxicological studies on carbathiin that would be applicable to females (13–50) or to the general population (including infants and children).		
Short (1–30 days) and intermediate-term (1–6 months) dermal exposure	NOAEL = 400 mg/kg/day	28-day dermal toxicity study in rats; based on kidney histopathological effects such as tubular degeneration and mineralization at the LOAEL = 1 000 mg/kg/day	100
Short-term inhalation exposure (1–30 days)	Oral NOAEL = 10 mg/kg/day	Based on a rat developmental gavage study that showed maternal treatment related decrease body weight, body weight gain and food consumption, and increase hair loss at LOAEL = 90 mg/kg/day	100
Intermediate-term inhalation exposure (1–6 months)	Oral NOAEL = 5.5 mg/kg/day	Based on 90 day rat subchronic oral toxicity study that showed histopathological changes in kidneys at LOAEL = 10.5 mg/kg/day	100
Chronic dietary (all populations)	Oral NOAEL = 0.8 mg/kg/day Chronic RfD = 0.008 mg/kg/day	Combined chronic / oncogenicity study in rats Male: LOAEL = 9mg/kg/day based on decreased body weight and body-weight gain, increased urine nitrogen and creatinine, increased water consumption and urine volume, decreased urine specific gravity, histopathological changes in kidneys Female: LOAEL = 16 mg/kg/day based on histopathological changes in kidneys	100
	Chronic PAD = 0.008 mg/kg/day (i.e. acceptable daily intake) FQPA SF = 1		

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

Appendix III Label Amendments for Products Containing Carbathiin

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 after the re-evaluation decision.

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

I) The following statements must be included in a section entitled **PRECAUTIONS:**

Dust/powder formulations:

All workers involved in treating seeds, clean-up, repair and maintenance of seed treatment equipment must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks and a dust mask. Baggers, sowers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks, and a dust mask to minimize exposure to dust from treated seeds.

Liquid formulations:

All workers involved in treating seeds, clean-up, repair and maintenance of seed treatment equipment must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks. Baggers, sowers and workers involved in handling treated seeds must wear a long-sleeved shirt and long pants, chemical-resistant gloves, shoes and socks, and a dust mask or appropriate respirator to minimize exposure to dust from treated seeds.

Oxycarboxin end-use products:

Do not re-enter or allow the re-entry into treated areas until 12 hours after application.

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

> In cleaning of equipment or disposing of wastes, do not contaminate water used for human or animal consumption or by wildlife and aquatic life or for irrigation purposes.
>
> Treated seed may be hazardous to birds and mammals. Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned-up from the soil surface.

III) The following statement must be included in section entitled **USE RESTRICTIONS:**

> DO NOT use treated seed for food, feed or oil processing.
>
> DO NOT contaminate food, feed, domestic or irrigation water supplies, lakes, streams and ponds.

All bags containing treated seed for sale or use in Canada must be labelled or tagged as follows:

> This seed has been treated with carbathiin. Wear a long-sleeved shirt, long pants and chemical-resistant gloves when handling treated seeds.
> DO NOT use for food, feed or oil processing. Store away from food and feed.

IV) The following soil treatment uses must be removed from the carbathiin end-use product label (i.e. Registration no. 13051) **bedding plants, bench plants and tree seedling treatment.**

References

List of Studies/Information Submitted by Registrant

PMRA 1464588 Technical Chemistry file - Carbathiin Vitavax –Confirmation of Source, Trace Organic Impurities, DACO: 2.99 (UV spectra, DACO 2.14.12)

PMRA 1464589 1992, Explanation of Certification of Ingredient Limits and Confidential
Statement of Formula and Confidential Attachment,
DACO: 2.12.1, DACO 2.13.3

PMRA 1464581 Technical Chemistry file - Carbathiin Vitavax Samples and Information Required for active Ingredients of Pesticide Products. Colorimetric Microdetermination of Vitavax (5,6-Dihydro-2-methyl-1,4-oxathiin-3-carboxanilide) Residues in Crops, DACO 2.14, DACO 2.11.3

PMRA 1620527 Oxycarboxin. Submission of Information Requested in Trade Memorandum T-1-212 Part 2. Submitted February 1, 1982. PTX-CRE-2, DACO 2.99

PMRA 1620529 Plantvax-75W (Oxycarboxin). Part 2. Submitted August 13, 1982. PTX-CRE-2, DACO 2.99