Proposed Re-evaluation Decision PRVD2011-07

Thiophanate-methyl

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Overview

What Is the Proposed Re-evaluation Decision?

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

Preliminary risk and value assessments for thiophanate-methyl were published in Re-evaluation Note REV2007-12, *Preliminary Risk and Value Assessments of Thiophanate-Methyl* (27 September 2007). The PMRA identified potential risks to the environment, to workers both during application and during re-entry activities and to the general population through drinking water exposure. By means of REV2007-12, the PMRA invited the public and all interested parties to submit information that could be used to refine the assessments and/or mitigate exposure risks.

Comments, data and information received in response to REV2007-12 were reviewed and used to revise the risk and value assessments, as necessary, and to propose regulatory action. Appendix I summarizes the comments received during the consultation process and provides the PMRA's response to these comments.

An evaluation of available scientific information found that products containing thiophanate-methyl do not present unacceptable risks to human health or the environment when used according to revised label directions. The PMRA is proposing a requirement for additional data and risk-reduction measures on labels to further protect human health and the environment, as a condition for continued registration

This proposal affects all end-use products containing thiophanate-methyl 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 thiophanate-methyl and presents the reasons for the proposed re-evaluation decision. 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 thiophanate-methyl.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

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

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

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

Thiophanate-methyl was re-evaluated under Program 2 which includes all products for which a Canadian regulatory decision requires a detailed in-house re-evaluation covering the full range of assessments of the risks to human health and the environment, as well as consideration of value. In particular, an assessment of efficacy may be performed where there is the need to reduce identified risks to human health and the environment through the reduction of use rates or frequency of use.

What is Thiophanate-methyl?

Thiophanate-methyl (TPM) is a broad spectrum, Resistance Management Group 1 (methyl benzimidazole carbamate) fungicide. Thiophanate-methyl is a systemic fungicide with protective and curative action. The systemic action of this fungicide results in disruption of fungal mitosis, and the mode of action is by inhibition of tubulin formation. The registered uses (not including emergency registrations) of thiophanate-methyl belong to the following use site categories: greenhouse non-food crops, terrestrial food crops, outdoor ornamentals (Commercial and Domestic Class products), turf and seed treatment for food and feed. It is applied by means of watering equipment, ground and aerial hydraulic sprayers, dry seed treatment container or seeder box, slurry machines or hand mixing with paddle or shovel, granular spreader and squeeze duster by farmers, farm and nursery workers, professional applicators, and residential gardeners. Carbendazim is the primary metabolite of thiophanate-methyl.

Health Considerations

Can Approved Uses of Thiophanate-Methyl Affect Human Health?

Thiophanate-methyl is unlikely to affect human health when used according to the revised label directions, which include additional risk-reduction measures. Potential exposure to thiophanate-methyl may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels at which no health effects occur in animal testing 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 the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

The cancer risk estimates include a number of conservative (health protective) assumptions that may overestimate exposure, and therefore risk. The application of the proposed mitigation measures reduces the risk for postapplication activities. Proposed protective measures to reduce worker exposure require consultation with user groups to determine their feasability and acceptability to the agricultural community. Additional data such as information on typical use pattern (typical rates, number of applications, survey information on critical worker activities that may take place during the application window, etc.) may also help to refine the current risk assessment and could reduce the proposed restricted-entry intervals.

To address most occupational concerns, additional risk-reduction measures are required on thiophanate-methyl labels. Thiophanate-methyl is unlikely to affect human health for workers when used according to the revised label directions. Most of these risk reduction measures are feasible but some are not. The PMRA is soliciting feedback on these proposed measures.

Non-cancer risks from drinking water exposure are not of concern. Potential cancer risk from drinking water exposure is uncertain, as estimates are based on conservative upper bound assumptions from water modelling. Once further information on the use pattern is considered, exposure from drinking water will be reassessed.

Residues in Food and Water

Dietary acute and chronic risks from food are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

The acute and chronic dietary (food only) exposures to thiophanate-methyl are less than the reference doses for all population subgroups. Therefore, acute and chronic dietary exposures to thiophanate-methyl are not of concern.

The acute and chronic dietary (food only) exposure to carbendazim, the primary metabolite of thiophanate-methyl, are less than the reference doses for all population subgroups. Therefore, acute and chronic dietary exposures to carbendazim are not of concern.

The lifetime cancer risk from food-only exposure to both thiophanate-methyl and carbendazim is not of concern.

Dietary risks from the acute and chronic aggregate exposures to food and drinking water to thiophanate-methyl and carbendazim are not of concern.

Potential concentrations of thiophanate-methyl and carbendazim in drinking water sources were estimated using modelling results only, as no reliable monitoring data were available. These modelled estimates are developed with a number of conservative assumptions and are generally considered to be upper-bound estimates. These drinking water estimates were combined with the food-only exposure to estimate the potential aggregate exposure from both food and drinking water.

The acute and chronic exposures to thiophanate-methyl from food and drinking water sources are less than the reference doses for all population subgroups. Therefore, acute and chronic dietary exposure to thiophanate-methyl are not of concern.

The acute and chronic exposures to carbendazim, the primary metabolite of thiophanate-methyl, from food and drinking water sources are less than the reference doses for all population subgroups. Therefore, acute and chronic dietary exposure to carbendazim are not of concern.

Lifetime cancer risk estimates exceed 1×10^{-6} when dietary (food-only) and drinking water exposures are aggregated.

The lifetime cancer risk from food and drinking water exposure to both thiophanate-methyl and carbendazim is estimated to be greater than 1×10^{-6}. However, the water modelling estimates used a number of conservative assumptions and are considered upper-bound estimates. Upon receipt of confimatory data requested in this PRVD, updated use pattern information including drift considerations, application rates, timing of application and regional scenarios will be used to revise the drinking water estimates.

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 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. Generally, food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

MRLs of thiophanate-methyl in or on food are currently established under the *Pest Control Products Act*. Canadian food crop uses include apples, cherries, dry common beans, lowbush blueberries, nectarines, peaches, pears, plums, potatoes (cut seed), prunes, raspberries, strawberries, sugar beets, sweet corn and white beans. The residue definition is methyl 1-(butylcarbamoyl)benzimidazol-2-ylcarbamate (benomyl), methyl benzimidazol-2-ylcarbamate (carbendazim) and 1,2-di-(3-methoxy-carbonyl-2-thioureido)benzene (thiophanate-methyl), expressed as carbendazim. These MRLs and the residue definition are common for the pesticides benomyl, carbendazim and thiophanate-methyl. 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.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern when used according to revised label directions.

Thiophanate-methyl is registered for use on residential roses, flowers, ornamentals and junipers. Cancer and non-cancer risk estimates associated with applying dusts to residential ornamentals are not of concern, if a new label statement is implemented limiting the use to 3 applications per year.

Non-occupational postapplication exposure may occur through gardening in treated areas or golfing on treated golf turf. Non-occupational postapplication risk is not of concern for gardeners and golfers, provided the maximum application rate for golf course turf is reduced, as proposed by the registrant.

Aggregate risk from exposure incurred as a patron of a "Pick Your Own" Orchard or Berry facility was not assessed.

"Pick Your Own (PYO)" facilities are considered commercial farming operations that allow public access for harvesting in large-scale fields or orchards treated with commercially labelled thiophanate-methyl products. Estimates of exposure that aggregate the dermal exposure incurred during harvest and the dietary exposure from consuming fresh fruit were not assessed for thiophanate-methyl.

Occupational Risks From Handling Thiophanate-methyl

The majority of occupational risks are not of concern provided additional mitigation measures are followed.

Occupational risk assessments consider exposure to workers who mix, load, and apply the pesticide. Most occupational risks are of concern for agricultural scenarios based on the current use pattern. However, if engineering controls and/or personal protective equipment are used, the majority of uses have no health concerns. These measures are needed to minimize potential exposure and protect worker's health. Regarding commercial seed treatment, additional data are required for continued registration, as risks to workers continue to be of concern after consideration of all feasible mitigation measures. For those uses that continue to have health risk concerns, further mitigation or consideration of removal of the use is needed.

Postapplication risks are not of concern provided additional mitigation measures are followed.

Postapplication occupational risk assessments consider exposures to workers entering treated sites in agriculture. Based on the current use pattern for agricultural scenarios reviewed for this re-evaluation, non-cancer and cancer postapplication risks to workers performing activities, such as thinning, pruning and harvesting of most crops, did not meet current standards and are of concern. However, when the proposed mitigation measures such as lengthened restricted-entry intervals (REIs), restricting the number of applications and lowering application rates are considered, the risks to postapplication workers are acceptable. Some of the proposed REIs are not considered agronomically feasible. The PMRA is requesting comments on the feasibility of the REIs. The generation of additional data may refine the current risk assessment and would be required to reduce the proposed REIs.

Environmental Considerations

What Happens When Thiophanate-Methyl Is Introduced Into the Environment?

The risk from thiophanate-methyl to birds and mammals is not a concern, given their mobile nature, and hence, reduced exposure. Thiophanate-methyl has negligible risk to aquatic organisms, except for risk to amphibians. The transformation product, methyl 2-benzimidzolylcarbamate (carbendazim) poses chronic risk to aquatic invertebrates. Additional risk reduction measures need to be observed.

As a result of the use of thiophanate-methyl outdoors, it can be found in soil and water. However, it is not persistent as it is rapidly broken down into the transformation product carbendazim. The latter persists in soil and water. Carbendazim adsorbs to soil and so is only slightly mobile in soil.

Foliar applications of thiophanate-methyl do not present an acute risk to birds at the maximum application rates used in agriculture (2 applications at 1.575 kg a.i./ha). However, at the higher application rates used on turf (12.25 kg a.i./ha), there is a risk to small birds when consumed in the diet. This conclusion was based on the conservative assumption that 100% of the diet is contaminated, when the birds are present in-field. However, given the mobile nature of birds the exposure would be less. When birds are present off-field, the risk from spray applications is negligible. With respect to reproductive effects in birds present in-field, the level of concern was not exceeded except at the application rates used on turf. Off-field, the reproductive risk was negligible. Granular applications of thiophanate-methyl which are used on turf, did not exceed the level of concern for acute risk, except for small birds the size of a sparrow.

Thiophanate-methyl when used in turf, poses an acute risk to small mammals present in-field but not when present off-field. Use in turf also poses a dietary risk to small mammals present in-field and at a reduced level off-field. The reproductive level of concern is exceeded particularly when used in turf to small mammals present in-field, but is negligible off-field. The assessment of risk to small mammals was also based on the conservative assumption that 100% of the diet is contaminated. Foliar applications of thiophanate-methyl do not pose a risk to bees present in-field, except at the application rates used on turf. The risk to bees is negligible off-field. It poses a risk to earthworms present in-field at nearly all application rates, while off-field the risk is negligible at all application rates, except mainly at the application rates used in turf.

A refined assessment of the risks to aquatic life indicates that thiophanate-methyl in runoff and spray drift is not a concern (acute or chronic) to fish at the application rates used in agriculture and on turf. Runoff and spray drift do not present an acute risk to aquatic invertebrates. However, the chronic risk level of concern for aquatic invertebrates is exceeded following exposure to the moderately persistent transformation product methyl 2-benzimidzolylcarbamate that is formed in the water from both runoff and spray drift of thiophanate-methyl. Thiophanate-methyl spray drift into aquatic habitat poses some risk to amphibians but risk is negligible from exposure through runoff. The risk to aquatic plants and algae from thiophanate-methyl from spray drift or from runoff is negligible.

Value Considerations

What is the Value of Thiophanate-methyl?

Thiophanate-methyl has a number of important uses when applied as a seed treatment or when applied by drench and foliar means.

Important fully registered uses of thiophanate-methyl include seed treatment use on dry common beans for the control of seed-borne anthrachnose, potato seed treatment for the control of several seed-borne and soil-borne diseases, and turf treatments for the control of several fungal diseases. Drench and foliar treatments are also important to the potted ornamentals industry for the control of several soil-borne and foliar plant diseases of ornamentals that need to be produced to very high quality standards, especially for export. The latter industry typically lacks effective alternatives. The floriculture industry produces high value crops and is a significant player in the horticultural segment of the economy of several Canadian provinces.

Thiophanate-methyl has been used extensively in agriculture and horticulture for over thirty years and is important in resistance management due to its systemic activity.

This active ingredient is still a component in the management of several diseases, allowing fungicide rotation to prevent or delay the development of fungicide resistance. Because of its systemic properties, its wide pest control spectrum and ease of use, thiophanate-methyl is of economic value to the seed potato, dry bean seed, greenhouse ornamental and turf industries, where it is an efficient and economical method of controlling several important diseases with a single application. Since thiophanate-methyl is a systemic active ingredient, unlike many alternative products, it allows for flexible methods of application and timing on many crops as the active ingredient is transported to the site of infection.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

Risk-reduction measures are being proposed to address potential risks identified in this assessment. These measures, in addition to those already identified on existing thiophanate-methyl product labels, are designed to further protect human health and the environment. The following additional key risk-reduction measures are being proposed.

Human Health

To protect mixer/loader/applicators:

- Additional protective equipment when mixing/loading and applying to all crops.
- * Packaging of all thiophanate-methyl products currently listed as wettable powders in water soluble packaging, except for those intended for seed treatment use.
- Limited amount of thiophanate-methyl used per day for several crops (white beans, outdoor ornamentals, greenhouse potted ornamentals, dry common beans on-farm seed treatment, potatoes on-farm cut seed treatment).
- * Restrictions on number of applications allowed per season.

To protect workers entering treated sites:

- Restricted-entry Intervals are required for all crops.
- * Turf use limited to golf course greens and tees only.
- * Restrictions on number of applications allowed per season.
- * Maximum turf rate reduced to 12.25 kg a.i./ha.

* These risk reduction measures were proposed by the Registrant and/or growers.

Environment

- Additional advisory statements to protect non-target species.
- Buffer zones for aquatic habitats.

What Additional Scientific Information Is Required?

Confirmatory data will be required under section 12 of the *Pest Control Products Act*. The registrants of thiophanate-methyl must provide data or an acceptable scientific rationale to the PMRA for the following requirements as listed in Appendix II.

Human Health

Worker exposure studies for the specific uses indicated:

- mixer/loader/applicator - passive dosimetry data or biological monitoring data for on-farm potato seed treatment and planting
- mixer/loader/applicator - passive dosimetry data or biological monitoring data for dry common beans and sweet corn on-farm planting
- mixer/loader/applicator - passive dosimetry data or biological monitoring data for commercial seed treatment (dry common beans and sweet corn)

Residue chemistry studies:

- Enforcement analytical methodology
- Inter-laboratory analytical methodology validation
- Multi-residue analytical methodology evaluation

Toxicology data are required:

- Developmental neurotoxicity in rats (DACO 4.5.14) for thiophanate-methyl
- Developmental neurotoxicity in rats (DACO 4.5.14) for carbendazim

PMRA also requires any other studies conducted in response to the EPA 2001 RED.

Next Steps

Before making a re-evaluation decision on thiophanate-methyl, 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, which 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.

The PMRA is requesting comments from registrants and grower groups on the feasibility of lower application rates, product packaging, additional protective equipment, limits to amount of product used per day, and restricted-entry intervals. Specifically, the PMRA is requesting comments on the proposed REIs as listed in Table 8.1.1.1 and the proposed turf restriction for use on golf course greens and tees only. The PMRA is also soliciting other possible risk mitigation proposals.

Other Information

At the time that the re-evaluation decision is made, the PMRA will publish an Evaluation Report on thiophanate-methyl in the context of this re-evaluation decision (based on the Science Evaluation of this consultation document. In addition, the test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

1.0 Introduction

Thiophanate-methyl (TPM) is a broad spectrum systemic fungicide with protective and curative action. It is classified as a Resistance Management Group 1 (methyl benzimidazole carbamate) fungicide. The mode of action is by inhibition of tubulin formation which disrupts fungal mitosis. TPM is registered for the following Use-Site Categories (not including emergency registrations): greenhouse non-food crops, terrestrial food crops, outdoor ornamentals (Commercial and Domestic Class products), turf and seed treatment for food and feed. It is applied by ground and aerial equipment. Thiophanate-methyl and its metabolite carbendazim, are structurally related to several other benzimidazole compounds.

Following the re-evaluation announcement for Thiophanate-methyl, the registrant of the technical grade active ingredient in Canada indicated its intention to provide continued support for uses currently registered in Canada.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Chemical name

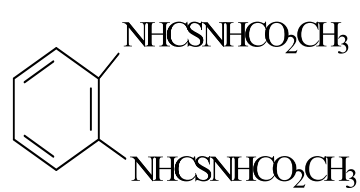
IUPAC Dimethyl 4,4'-(*o*-phenylene)bis(3-thioallophanate)

CAS Dimethyl [1,2-phenylenebis(iminocarbonothioyl)]bis[carbamate]

CAS number 23564-05-8

Molecular formula $C_{12}H_{14}N_4O_4S_2$

Structural formula



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

No impurities 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*, nor any Toxic Substances Management Policy (TSMP) Track 1 substances identified in Appendix II of Regulatory Directive DIR99-03 are expected to be present in the starting materials used to manufacture the product nor are they expected to be formed during the manufacturing process.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Colour	colourless
Physical state	crystals
Odour	faint sulphur odour
Melting point/range	172°C (decomp.)
Boiling point/range	not applicable
Density or specific gravity	1.4–1.6
Water solubility at 23°C	Practically insoluble in water
Solvent solubility at 23°C	Solvent — Solubility (g/kg) acetone 58.1 cyclohexanone 43 methanol 29.2 chloroform 26.2 acetonitrile 24.4 ethyl acetate 11.9 slightly soluble in hexane
Vapour pressure at 25°C	0.0095 mPa
n-Octanol–water partition coefficient (K_{ow})	log K_{ow} = 1.5
Dissociation constant (pK_a)	pKa= 7.28

2.3 Description of Registered Thiophanate-Methyl Uses

Appendix III lists all thiophanate-methyl products that are registered under the authority of the *Pest Control Products Act* that are supported by the registrant. Appendix IVa and IVb list all the Commercial and Domestic Class uses respectively, for which thiophanate-methyl is presently registered that are still supported by the registrant. All supported uses were considered in the health and environmental risk assessments of thiophanate-methyl. Also presented is whether the use was added through the PMRA Minor Use Label Expansion (URMULE) program. While currently supported by the registrant, the data supporting the minor use was originally generated by a user group.

Currently registered uses of thiophanate-methyl that are still supported by the registrant belong to the following use site categories: greenhouse non-food crops, terrestrial food crops, outdoor ornamentals (Domestic and Commercial Class products), turf and seed treatment for food and feed.

3.0 Impact on Human Health

3.1 Toxicology Summary

The toxicology data base for both thiophanate-methyl and carbendazim is based primarily on registrant-supplied data. Available published studies were also considered. Both carbendazim and thiophanate-methyl were of low acute toxicity by oral and dermal administration in various laboratory animal species, and of low (carbendazim) or slight (thiophanate-methyl) toxicity by the inhalation route. Clinical signs of acute oral and inhalation thiophanate-methyl toxicity included tremors, increased sensitivity to touch, clonic/tonic convulsions, ataxia and ptosis. Liver pathology, testicular and spermatogenic effects were noted in acute studies with carbendazim. Carbendazim and thiophanate-methyl were minimally or non-irritating to eyes and skin. Thiophanate-methyl was a skin sensitizer in the Guinea pig, whereas carbendazim was negative. Both thiophanate-methyl and carbendazim undergo rapid systemic absorption and distribution following oral exposure, with greater than 80% excretion via the urine and faeces within 24 hours. Tissue retention was minimal, with the liver and kidney showing the highest tissue concentrations for both compounds, in addition to the thyroid for thiophanate-methyl. Thiophanate-methyl is metabolized by hydroxylation and hydrolysis to carbendazim, which is further metabolized to 5-methoxycarbendazim sulfate, the major urinary metabolite. The major carbendazim metabolite is 5-hydroxy-2-benzimidazole carbamate.

In short and long-term animal toxicity studies, the liver was the primary target for both compounds. Thiophanate-methyl produced additional effects in the thyroid and kidney, and carbendazim also induced testicular toxicity. The dog was the species most sensitive to thiophanate-methyl-induced thyroid hormone effects. Potential evidence of neurotoxicity at high dose levels was noted in a 1-year study in dogs, based on tremors occurring within two to four hours of dosing, and in a two-generation reproduction study in which post-weanling male pups showed reduced performance in an open-field test. The neurotoxic effects of carbendazim were limited to mild transient effects that occurred at high doses only, without histological evidence of neuropathy. Both thiophanate-methyl and carbendazim induced liver tumours in male and female mice. Thiophanate-methyl also induced thyroid tumours in male rats, and ovarian granulosa cell tumours and leuteomas were noted in one strain of mice treated with carbendazim. Carbendazim and thiophanate-methyl were not mutagenic, but are well known aneugens, with carbendazim inducing aneugenic effects at lower doses than thiophanate-methyl. However, 2-aminobenzimidazole, a minor metabolite of both carbendazim and thiophanate-methyl was mutagenic, and thiophanate-methyl and some of its metabolites share a thiourea moiety that is implicated in thyroid tumour formation.

Resorptions, craniofacial and/or rib malformations were observed in carbendazim-treated rats, rabbits and hamsters in the absence of maternal toxicity in all species tested, indicating fetal sensitivity. More severe effects occurred as a result of gavage dosing compared to dietary administration, although fetal sensitivity was noted with both routes. Thiophanate-methyl is metabolised to carbendazim, yet the developmental effects induced by thiophanate-methyl were less severe than those induced by carbendazim. Multiple supernumery ribs in rabbit fetuses were noted at maternally toxic doses of thiophanate-methyl. Developmental concerns regarding thiophanate-methyl stem from the fact that short and long-term exposures to thiophanate-methyl caused decrements in circulating thyroid hormones in rats, mice and dogs. Adequate circulating levels of thyroid hormones are critical for normal development of the mammalian fetal and neonatal brain and persistent decreases in thyroid hormone levels increase the potential for neurodevelopmental deficits in the young. Thus, a developmental neurotoxicity study is warranted. No reproductive toxicity was observed with either compound in guideline studies, however, a number of published and unpublished studies on carbendazim reported sperm and testicular changes (inhibition of spermatogenesis and sperm reduction, germinal epithelium degeneration, lower testis weight) with high-dose, short-term gavage and dietary dosing.

Reference doses were established for each compound based on NOAELs for the most relevant endpoints. These included neurotoxic symptoms, developmental toxicity, and thyroid effects for thiophanate-methyl; and sperm effects, developmental toxicity and systemic toxicity for carbendazim. These reference doses incorporate uncertainty factors to account for extrapolating between animals and humans, and for variability within human populations. Additional uncertainty factors were also applied to take into consideration the severity of effects, fetal sensitivity and any residual uncertainties in either database. Quantitative cancer risk assessments were conducted for both thiophanate-methyl and carbendazim-induced mouse liver tumours.

The toxicology endpoints used in the risk assessment of thiophanate-methyl and carbendazim are summarized in Appendix V (Tables 1 and 2, respectively). The uncertainty factors have not been revisited since the Science Policy Note (SPN 2008-01), *The Application of Uncertainty Factors and the Pest Control Products Act Factor in the Human Health Risk Assessment of Pesticides*, was published. However, they will be reassessed upon receipt and assessment of all new toxicology data.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive human population. 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.

Where evidence of carcinogenicity is identified for the active ingredient, a cancer potency factor (Q_1*) is generated and used to estimate cancer risk. The product of the expected exposure and the cancer potency factor (Q_1*) estimates the lifetime cancer risk as a probability. A lifetime cancer risk of 1×10^{-5} in worker populations and 1×10^{-6} in the general population is generally considered acceptable.

3.2.1 Toxicology Endpoint Selection for Occupational and Residential Risk Assessment

3.2.1.1 Short-, intermediate-, and long-term dermal and inhalation endpoint(s)

THIOPHANATE METHYL (TPM)

To estimate the risk from **short-term dermal exposure** to thiophanate-methyl (<30 days), a **NOAEL of 100 mg/kg bw/day** from a 21-day dermal study in rabbits was selected. This NOAEL was based on decreased body weight and food consumption at 300 mg/kg bw/day. The **target margin of exposure (MOE) is 300.** This accounts for interspecies extrapolation (10×) and intraspecies variability (10×) with an additional factor (3×) for the lack of acute, subchronic and developmental neurotoxicity studies. Since a dermal NOAEL is used, no dermal absorption factor is required for route-to-route extrapolation.

To estimate the risk from **short-term inhalation exposure** to thiophanate-methyl (<30 days), a **NOAEL of 10 mg/kg bw/day** from a rabbit developmental toxicity study was selected. An oral endpoint was used as a repeat-dose inhalation study was not available. The NOAEL was based on decreased maternal body weight and food consumption at the LOAEL of 20 mg/kg bw/day. **The target margin of exposure (MOE) is 300**. This accounts for interspecies extrapolation (10×) and intraspecies variability (10×) with an additional factor (3×) for the lack of acute, subchronic and developmental neurotoxicity studies. Since an oral NOAEL is used, an inhalation absorption factor of 100% is assumed for route-to-route extrapolation.

To estimate the risk from **intermediate-term (1-6 months) and long term (> 6 months) dermal and inhalation exposures** to thiophanate-methyl, a **NOAEL of 8 mg/kg bw/day** from a 1-year dog and a 2-year rat study was selected, based on increased thyroid weight and decreased serum thyroxine in male dogs at 40 mg/kg bw/day, testicular atrophy and reduced thyroid follicular cell colloid in male rats at 32 mg/kg bw/day, and thyroid follicular cell hypertrophy and reduced body weight gain in both species. This is supported by a NOAEL of 8.8 mg/kg bw/day from a second 2-year dietary study in rats, based on thyroid, kidney and liver effects, increases in serum TSH and cholesterol levels and decreased thyroid hormone levels in rats at 54.4 mg/kg bw/day. The **target margin of exposure (MOE) is 1000**. This accounts for interspecies extrapolation (10×) and intraspecies variability (10×) with additional factors for the use of an endocrine endpoint (3× thyroid effects) and for residual uncertainties concerning potential neuroendocrine sensitivity in the young due to possible thyroid interactions (3×).

Risks from carbendazim, the primary metabolite of thiophanate-methyl, are also considered in the postapplication assessment.

CARBENDAZIM (CAZ)
To estimate the risk from **short- to intermediate-term dermal and inhalation exposure** to carbendazim (< 6 months), a **NOAEL of 10 mg/kg bw/day** from both rat and rabbit developmental toxicity studies was selected. An oral endpoint was used, as a repeat-dose dermal study did not address the endpoint of concern noted in the oral developmental studies. This NOAEL was based on an increased incidence of fetal malformations at the LOAEL of 30 mg/kg bw/day in rats and increased resorptions at the LOAEL of 20 mg/kg bw/day in rabbits, both in the absence of maternal toxicity. The **target MOE is 1000** to account for interspecies extrapolation (10×) and intraspecies variability (10×), with an additional factor of 10× for fetal sensitivity and severity of effects (malformations in the absence of maternal toxicity), and the lack of a developmental neurotoxicity study. This endpoint and target MOE is also protective of the sperm effects noted in rats after receiving a single oral dose. Since an oral NOAEL is used, dermal and inhalation absorption factors are required for route-to-route extrapolation.

The toxicology endpoints used in the risk assessment of thiophanate-methyl and carbendazim are summarized in Appendix V (Tables 1 and 2, respectively).

3.2.1.2 Cancer Potency Factor

THIOPHANATE METHYL
A quantitative risk assessment for tumorigenicity was conducted based on increased hepatocellular tumours in male mice. Female mice also had an increase in liver tumours. A cancer potency factor (Q_1*) of 1.32×10^{-2} (mg/kg bw/day)$^{-1}$ was utilized.

CARBENDAZIM
A quantitative risk assessment for tumorigenicity was conducted based on increased hepatocellular tumours in female mice. An increase in liver tumours was also noted in male mice. A cancer potency factor (Q_1*) of 1.6×10^{-2} (mg/kg bw/day)$^{-1}$ was utilized .

3.2.1.3 Dermal Absorption

THIOPHANATE METHYL
A dermal absorption value of 25% was chosen for the re-evaluation of thiophanate-methyl based on the apparent dermal absorption, the physical-chemical properties and the in vitro study submitted to the PMRA.

CARBENDAZIM
A dermal absorption value of 25% was chosen for the carbendazim portion of the re-evaluation of thiophanate-methyl based on the physical-chemical properties and by a comparison of these properties to a structurally-related compound which has similar toxicological effects (i.e. benomyl which has a chemical specific dermal absorption study available).

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to thiophanate-methyl through mixing, loading or applying the pesticide, and when entering a treated site to conduct activities such as scouting and/or irrigating treated crops.

3.2.2.1 Mixer, Loader and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders, and applicators. The following scenarios were assessed:

- Mixing/loading water soluble bags.
- Aerial application to lowbush blueberries and white beans.
- Groundboom application to berries, white beans, sugar beets, outdoor ornamentals and turf.
- Low pressure handwand and backpack application to aspen and poplar, greenhouse potted ornamentals, berries, outdoor ornamentals and turf.
- High pressure handwand application to aspen and poplar, greenhouse potted ornamentals and outdoor ornamentals.
- Airblast application to aspen and poplar, stone fruits and outdoor ornamentals.
- Right-of-way sprayer for aspen and poplar.
- Push rotary spreader and tractor drawn spreader to turf.
- Ready-to-use (shaker can) for roses, flowers and evergreens (residential).
- Slurry machines and hand mixing for application to dry common beans.
- Seed box treatment to sweet corn.
- Convenient container or by dust attachment over belt application to cut seed potatoes.

Based on the number of applications and timing of application, workers applying thiophanate-methyl would generally have a short-term (<30 days) duration of exposure. Exceptions would be for the following:

- ornamentals;
- turf (for the granular formulation and the lower rate in water soluble bags);
- dry bean and sweet corn seed treatment (commercial); and
- greenhouse potted ornamentals.

The PMRA estimated handler exposure based on different levels of personal protection:

- Mid-level PPE: coveralls over long sleeved shirt and long pants, chemical resistant gloves, with and without respirator.

- Maximum PPE: chemical resistant coveralls over long sleeves and long pants, chemical resistant gloves and a respirator.

- Engineering controls: Represents the use of an appropriate engineering control such as closed tractor cab or closed loading system (water soluble packages).

No chemical-specific handler exposure data were submitted for thiophanate-methyl, and therefore dermal and inhalation exposures were estimated using data from the *Pesticide Handlers Exposure Database (PHED), Version 1.1*. The PHED is a compilation of generic mixer/loader applicator passive dosimetry data with associated software which facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of personal protective equipment (PPE). In most cases, PHED did not contain appropriate data sets to estimate exposure to workers wearing coveralls, chemical resistant coveralls or a respirator. This was estimated by incorporating a 75% clothing protection factor for coveralls, a 90% clothing protection factor for chemical resistant coveralls and a 90% protection factor for a respirator into the unit exposure data. Similarly, a 90% protection factor was applied to head and neck dermal unit exposure values for chemical resistant head-gear. Chemical resistant head gear includes so'westers, or large brimmed, water-proof hats, and hoods with sufficient neck protection.

The Outdoor Residential Exposure Task Force (ORETF) also generated several useful exposure studies which monitored exposure of workers mixing, loading and applying pest control products to residential turf and gardens.

Thiophanate-methyl is registered for on-farm seed treatment use on sweet corn, dry beans and potato cut seed (short-term exposure), as well as in commercial seed treatment facilities (intermediate-term exposure). PHED was not used to estimate exposure since PHED is not considered representative for this exposure scenario. For treating sweet corn and dry bean seed on farm, the unit exposure numbers were from a published study (Fenske et *al.*, 1990). The study only monitored the actual treating of seed; seed was not planted as part of the study and clean-up activities were also not monitored.

The registrant does not currently have access to any commercial seed treatment studies. USEPA Policy 14 values were cited only to indicate that target MOEs for commercial seed treatment for corn and dry beans may not be reached. USEPA Policy 14 is comprised of studies using wet formulations or wettable powder in water soluble bags.

A published study by Stevens and Davis (1981) was used to assess the potato cut seed exposure. However, this study had several limitations, which included the small number of replicates (3-18 for various job functions), only summary data available, monitoring periods were short (maximum of 2 hours), there was no quality assurance/quality control data and personal protective equipment was not detailed. As well, PMRA could not verify any of the study results as raw data was not reported.

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment might be refined with exposure data more representative of modern application equipment and engineering controls. Biological monitoring data might also further refine the assessment.

3.2.2.1.1 Occupational Exposure Non-Cancer Risk Estimates

Calculated MOEs exceed target MOEs for application, mixing and loading for the majority of uses, provided engineering controls or personal protective equipment are used as summarized below. Tables 1 and 2, of Appendix VI summarize the calculated MOEs for mixers/loaders and applicators.

Calculated MOEs are less than target MOEs for commercial seed treatment of dry common beans and seed corn, even after consideration of more feasible engineering controls and PPE.

For on-farm seed treatment (sweet corn and dry common bean), only mixing/loading and application to treated seeds was assessed. There was no data to assess planting treated seed. By limiting the amount of seed treated for dry beans the resulting MOE of 400 is considered sufficient to encompass the potential exposure from planting treated seed. A study to fill this data gap would be required for continued registration. Data from the Agricultural Handler Exposure Task Force (AHETF) may fill this data gap.

For potato cut seed, in order to reach the target MOE of 300, the maximum amount of cut seed handled per day would need to be limited to 10 000 kg. PPE was not specified in the study (Stevens and Davis, 1981), therefore, the label will require: coveralls over long sleeved shirt and long pants, chemical resistant gloves, and a dust/mist filtering respirator. Due to the low confidence in the published study used to assess exposure for potato cut seed treatment, a study to fill this data gap would be required for continued registration.

3.2.2.1.2 Occupational Exposure Cancer Risk Estimates

To estimate cancer risk, exposure was amortised over a lifetime to estimate a lifetime average daily dose (LADD). It was assumed that the maximum number of yearly applications is made at the maximum label rate, and that a working lifetime comprises 35 years of a 70-year life span.

Lifetime cancer risk estimates associated with mixing/loading/applying thiophanate-methyl for the majority of occupational handlers are not of concern provided additional PPE or engineering controls are used as summarized below. Table 3 of Appendix VI summarizes the calculated cancer risks for mixers/loaders and applicators.

Calculated cancer risks are greater than the target for commercial seed treatment of dry common beans and seed corn, even after consideration of more feasible engineering controls (e.g. PPE). A lifetime cancer risk of 1×10^{-5} in worker populations is generally considered acceptable. Sweet corn (commercial seed treatment) and dry common beans (commercial seed treatment) each had a cancer risk of 2×10^{-5} and were therefore of concern.

3.2.2.2 Postapplication Worker Exposure and Risk Assessment

The postapplication occupational risk assessment considered exposures to workers entering treated sites. Based on the thiophanate-methyl use pattern, there is potential for short- to intermediate-term (<6 months) postapplication exposure to thiophanate-methyl residues for workers.

Carbendazim, the primary metabolite of thiophanate-methyl, is also considered in the postapplication assessment for non-cancer and cancer risks.

All submitted chemical-specific dislodgeable foliar residue (DFR) and turf transferable residue (TTR) data were considered. Due to uncertainties in the percentage of thiophanate methyl that degrades to carbendazim at any time in the environment, 15% was selected to apply to the DFR/TTR data of thiophanate-methyl based on submitted DFR/TTR studies. Activity specific transfer coefficients (TC) were used to estimate postapplication exposure resulting from contact with treated turf and foliage at various times after application. DFR and TTR refer to the amount of residue that can be dislodged or transferred from a surface, such as the leaves of a plant or turf. A TC is a factor that relates worker exposure to dislodgeable residues. TCs are specific to a given crop and activity combination (e.g. hand harvesting apples, scouting late season corn) and reflect standard work clothing worn by adult workers. Postapplication exposure activities include (but are not limited to): scouting and mowing in turf; as well as hand harvesting, pinching, pruning, and thinning for ornamental and agricultural crops.

3.2.2.2.1 Postapplication Worker Non-Cancer Exposure and Risk Assessment

For workers entering a treated site, restricted-entry intervals (REIs) are calculated to determine the minimum length of time required before people can safely enter after application. An REI is the duration of time that must elapse before residues decline to a level where performance of a specific activity results in exposures above the target MOE (i.e. >300 for short-term dermal and >1000 for intermediate/long-term dermal exposure scenarios for thiophanate-methyl and >1000 for all dermal exposure scenarios for carbendazim).

To achieve the target MOEs for postapplication workers in agricultural scenarios, most current REIs would need to significantly increase in length or new REIs would need to be added to the label. Appendix VI summarizes the calculated REIs based on thiophanate-methyl (Table 4) and based on carbendazim (Table 5). Since postapplication exposure to thiophanate-methyl results in REIs being proposed, the DFR/TTR residue data on the day of the proposed REI for thiophanate-methyl is used in the carbendazim assessment. If necessary, the REI was increased until the carbendazim risk was acceptable.

The proposed REIs may not be agronomically feasible.

3.2.2.2.2 Postapplication Worker Cancer Exposure and Risk Assessment

Postapplication cancer risks for postapplication workers were based on average residues for 7 or 30 days, starting on the day of the recommended REI required to meet the target MOE discussed previously.

A cancer risk less than or equal to 1×10^{-5} is considered acceptable for occupational scenarios. Occupational postapplication cancer risk for thiophanate-methyl and carbendazim separately and combined is less than 1×10^{-5} for all uses except greenhouse potted ornamentals (all activities) (Appendix VI, Tables 6 and 7). However, an application method in greenhouses that involved no contact with the foliage (i.e. soil drench) would be acceptable as dermal postapplication exposure would be minimal. Under these conditions, a 12hr REI is required for greenhouse potted ornamentals.

3.2.3 Non-Occupational Exposure and Risk Assessment

Residential risk assessment estimates risks to the general population, including children/youths, during or after pesticide application.

Homeowners have potential for short-term (1-30 days) exposure to thiophanate-methyl during application of a dust formulation to roses, evergreens, conifers and other ornamentals, flowers and shrubs. Residential exposures have been estimated based on label application frequency, estimated seasonal length, and the persistence of thiophanate-methyl. It is estimated that thiophanate-methyl could be applied up to 3 times in a season to ornamentals by homeowners.

3.2.3.1 Residential Mixer, Loader and Applicator Exposure and Risk Assessment

Exposure estimates for residential applicators are based on Outdoor Residential Exposure Task Force (ORETF) data. For the residential scenario, the exposure estimates assume that individuals wear short pants, short sleeves and no gloves.

The calculated MOE for short-term exposure risk exceeds the target MOE for application, mixing and loading for the current label use (roses, evergreens, conifers and other ornamentals flowers and shrubs) and, therefore, is not of concern (Appendix VII, Table 1).

The lifetime cancer risk associated with mixing/loading/applying thiophanate-methyl for residential handlers is estimated as 1×10^{-6} (Appendix VII, Table 1). A lifetime cancer risk of 1×10^{-6} for the general population is generally considered acceptable. A label statement is required to ensure that use is limited to 3 times per year because additional applications will result in unacceptable cancer risk.

3.2.3.2 Residential Postapplication Exposure and Risk Assessment

Two groups, adults and youths, are potentially exposed (short-term) to thiophanate-methyl and carbendazim after application of thiophanate-methyl products in residential settings (after treatment to ornamentals) and golf courses (after treatment on turf).

Postapplication non-cancer risk for gardeners is based on a DFR study and postapplication non-cancer risk for golfers is based on the highest reported TTR value. Calculated MOEs for thiophanate-methyl and carbendazim postapplication non-cancer risk estimates exceed their target MOEs for gardeners and golfers (youth and adults) and are therefore not of concern (Appendix VII, Tables 2 and 3).

Cancer risk estimates are assessed based on the 7-day average DFR or TTR data following the day after treatment (day 0). The homeowner cancer risk from postapplication contact with treated ornamentals during gardening or other activities is not of concern for thiophanate-methyl and carbendazim. (Appendix VII, Tables 2, 3 and 4). The golfer cancer risk from postapplication contact with treated turf during golfing is not of concern for thiophanate-methyl and carbendazim (Appendix VII, Tables 2, 3 and 4), provided that the maximum turf rate is reduced as proposed by the registrant.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in fruits, vegetables, milk, meat, eggs and processed products, may be ingested with the daily diet. These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children’s eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. Health Canada’s Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides, A User’s Guide*, presents detailed acute and chronic risk assessment procedures.

Residue estimates used in the dietary risk assessment may be conservatively based on the maximum residue limits (MRLs) or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency’s National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program (PDP). Specific and empirical processing factors as well as specific information regarding percent of crops treated may also be incorporated to the greatest extent possible.

Acute, chronic, and cancer dietary exposure and risk assessments were conducted for thiophanate-methyl using the Dietary Exposure Evaluation Model – Food Commodity Intake Database™ (DEEM-FCID™, Version 2.03), which incorporates consumption data from the United States Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994 to 1996 and 1998. The analyses were performed to support the re-evaluation eligibility for continuing registration for thiophanate-methyl and its metabolite carbendazim (CAZ). Carbendazim is not registered for use on food crops; however, thiophanate-methyl degrades to carbendazim, and both are identified as residues of concern. Dietary exposures to thiophanate-methyl and carbendazim were independently estimated and assessed against chemical specific endpoints. The non-cancer endpoints for thiophanate-methyl and carbendazim differed, therefore exposure to thiophanate-methyl and carbendazim were assessed independently. The cancer assessment for both thiophanate-methyl and carbendazim had a common endpoint, and therefore the exposure and risk estimates were combined.

The dietary exposure and risk estimates for thiophanate-methyl and carbendazim are summarized in Appendix VIII (Table 1).

3.3.1 Determination of Acute Reference Dose

THIOPHANATE-METHYL

To estimate acute dietary risk (1 day) for the general population, including infants and children, an acute dietary reference dose (ARfD) was set at 0.13 mg/kg bw. This was based on a NOAEL of 40 mg/kg bw/day for tremors that occurred within 2-4 hours of dosing at 200 mg/kg bw/day in a 1-year study in dogs. An uncertainty factor of 300 was applied to account for inter-species extrapolation (10×), intra-species variability (10×), and lack of an acute neurotoxicity study in rodents (3×). Neurotoxicity studies are required, based on evidence for potential neurotoxic effects in the database.

For females 13 to 49 years of age, an ARfD was set at 0.067 mg/kg bw. This was based on a fetal NOAEL of 20 mg/kg bw/day for multiple supernumerary ribs in a rabbit developmental study at 40 mg/kg bw/day. This effect is considered relevant to a single-dose exposure during pregnancy. An uncertainty factor of 300 was applied to account for inter-species extrapolation (10×), intraspecies variability (10×), and the lack of acute neurotoxicity and developmental neurotoxicity studies, which are required based on evidence for potential neurotoxic effects in the database (3×).

CARBENDAZIM

To estimate acute dietary risk (1 day) for males, a LOAEL of 50 mg/kg bw was selected. This was based on a published study on the acute testicular effects of carbendazim in rats, where an absence of immature germ cells with round spermatids (stage I and II), and elongated spermatids sloughed from stage VII epithelium were noted on day 2 post-treatment. An overall uncertainty factor of 1000 is required to account for interspecies extrapolation (10×) and intraspecies variability (10×), 3× for the use of a LOAEL and 3× for seriousness of effect. This effect can be irreversible at higher doses, and the capacity for reversal at 50 mg/kg bw is unknown. The ARfD was calculated to be 0.05 mg/kg bw (50 mg/kg bw ÷ 1000).

To estimate acute dietary risk (1 day) in females 13 to 49 years of age, a NOAEL of 10 mg/kg bw/day from rat and rabbit developmental toxicity studies on carbendazim was selected. This NOAEL was based on an increased incidence of fetal malformations at 30 mg/kg bw/day in rats and increased resorptions at 20 mg/kg bw/day in rabbits, both in the absence of maternal toxicity. An overall uncertainty factor of 1000 is required to account for interspecies extrapolation (10×) and intraspecies variability (10×), with an additional factor of 10× for fetal sensitivity and seriousness of effects (malformations in the absence of maternal toxicity), and the lack of a developmental neurotoxicity study. The ARfD for females 13 to 49 years of age was calculated to be 0.01 mg/kg bw (10 mg/kg bw/day ÷ 1000).

3.3.2 Acute Dietary Exposure and Risk Assessment (thiophanate-methyl)

Acute dietary exposure is calculated considering the highest ingestion of thiophanate-methyl 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 thiophanate-methyl residue that may be consumed in a day. To determine acute dietary risks, a value representing the high end (99.9^{th} percentile) of this distribution is compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD the expected intake is not considered to be a health concern.

The acute dietary exposure was calculated using highly refined residue estimates based on food surveillance and plant metabolism data. Acute dietary exposure as a percentage of the reference dose is 3.1% for the most affected population of infants and 0.5% for females of reproductive age. The acute dietary exposure to thiophanate-methyl is less than the reference dose for all population subgroups; therefore, it is not of concern.

3.3.3 Acute Dietary Exposure and Risk Assessment (carbendazim)

The acute dietary exposure was calculated using highly refined residue estimates based on food surveillance and plant metabolism data. Acute dietary exposure as a percentage of the reference dose is 6.3% for the most affected population of infants, and 3.6% for females of reproductive age. The acute dietary exposure to carbendazim is less than the reference dose for all population subgroups; therefore, it is not of concern.

The acute exposure and risk assessment of thiophanate-methyl and carbendazim are summarized in Appendix VIII (Table 1).

3.3.4 Determination of Acceptable Daily Intake

THIOPHANATE-METHYL

To estimate the risk from chronic dietary exposure to thiophanate-methyl, a NOAEL of 8 mg/kg bw/day from a 1-year dog and a 2-year rat study with thiophanate-methyl was selected, based on increased thyroid weight and decreased serum thyroxine in male dogs at 40 mg/kg bw/day, testicular atrophy and reduced thyroid follicular cell colloid in male rats at 32 mg/kg bw/day, and thyroid follicular cell hypertrophy and reduced body weight gain in both species. This is supported by a NOAEL of 8.8 mg/kg bw/day from a second 2-year dietary study with thiophanate-methyl in rats, based on thyroid, kidney and liver effects, increases in serum TSH and cholesterol levels and decreased thyroid hormone levels in rats at 54.4 mg/kg bw/day. An overall uncertainty factor of 1000 is required to account for interspecies extrapolation (10×) and intraspecies variability (10×), 3× for the use of an endocrine endpoint (thyroid effects) and 3× for residual uncertainties concerning potential neuroendocrine sensitivity in the young due to possible thyroid interactions. The ADI was calculated to be 0.008 mg/kg bw/day (8 mg/kg bw ÷ 1000). This value was considered protective of all populations exposed to thiophanate-methyl.

CARBENDAZIM
To estimate the risk from chronic dietary exposure to carbendazim, an ADI was set at 0.009 mg/kg bw/day. A NOAEL of 9 mg/kg bw/day from a 2-year dietary study in dogs was selected, based on reduced body weight gain, increased alkaline phosphatase, reduced clotting time, increased organ/bw ratio (liver, pituitary, thyroid), and testicular effects (atrophic tubules, inflammatory cell infiltration) at 81 mg/kg bw/day. An overall uncertainty factor of 1000 was applied to account for interspecies extrapolation (10×) and intraspecies variability (10×), with an additional factor of 10× for fetal sensitivity and seriousness of effects in the absence of maternal toxicity in both the rat and rabbit developmental studies and the lack of a developmental neurotoxicity study.

3.3.5 Chronic Dietary Exposure and Risk Assessment (thiophanate-methyl)

Chronic dietary exposure is calculated using the average consumption of different foods and average residue values on those foods over a lifetime. This expected intake of residues is compared to the ADI, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the expected intake from residues is less than the ADI, this intake is not considered to be of concern.

As with the acute dietary risk assessment, the chronic dietary exposure and risk assessment for thiophanate-methyl used highly refined residue estimates based on food surveillance and plant metabolism data. Chronic dietary risk is less than 0.9% of the ADI for all population subgroups; therefore, it is not of concern.

3.3.6 Chronic Dietary Exposure and Risk Assessment (carbendazim)

As with the acute dietary risk assessment, the chronic dietary exposure and risk assessment for carbendazim used highly refined residue estimates based on food surveillance and plant metabolism data. Chronic dietary risk is less than 0.8% of the ADI for all population subgroups; therefore, it is not of concern.

The chronic exposure and risk assessment of thiophanate-methyl and carbendazim are summarized in Appendix VIII (Table 1).

3.3.7 Determination of Cancer Potency Factor

For thiophanate-methyl a quantitative risk assessment for tumorigenicity was conducted based on increased hepatocellular tumours in male mice. For carbendazim, female mice also had an increase in liver tumours. A cancer potency factor (Q_1*) of 1.32 × 10^{-2} (mg/kg bw/day)$^{-1}$ and of 1.6 × 10^{-2} (mg/kg bw/day)$^{-1}$ was utilized for thiophanate-methyl and carbendazim, respectively.

3.3.8 Carcinogenic Dietary Exposure and Risk Assessment (thiophanate-methyl and carbendazim)

The cancer risk from dietary exposure to thiophanate-methyl and the carbendazim metabolite are estimated using the chronic dietary exposure and the Q_1* for the respective chemicals. As these share a common cancer endpoint, the risk estimates were combined to give the total lifetime dietary risk. The food-only cancer risk is 5.5 × 10^{-7}. This cancer risk is less than 1 × 10^{-6}. A lifetime cancer risk that is below 1 × 10^{-6} usually does not indicate a concern for the general population.

3.4 Exposure From Drinking Water (thiophanate-methyl and carbendazim)

Drinking water exposure was assessed by calculating drinking water levels of comparison (DWLOC) and comparing these target values to the drinking water estimated environmental concentration (EEC).

3.4.1 Determination of Drinking Water Level of Comparison (DWLOC)

DWLOC generally expresses the difference between the reference dose and the non-drinking water exposure (i.e. food and residential exposures). In this assessment, DWLOC simply expresses the difference between the reference dose and the food-only exposure.

For thiophanate-methyl, the chronic DWLOCs ranged from 80 µg/L for infants to 280 µg/L for the general population. The acute DWLOCs ranged from 1260 µg/L for infants to 4540 µg/L for adults aged 20-49 years.

For carbendazim, the chronic DWLOCs ranged from 90 µg/L for infants to 315 µg/L for adults and youths. The acute DWLOCs ranged from 468 µg/L for infants to 1738 µg/L for male adults aged 20-49 years.

To determine the cancer DWLOC, the lifetime exposure in the general population to thiophanate-methyl and carbendazim were combined. The cancer DWLOC was then calculated to be 1 µg/L, expressed as carbendazim equivalents.

The acute, chronic and cancer DWLOC of thiophanate-methyl and carbendazim are summarized in Appendix VIII (Table 4).

3.4.2 Determination of Potential Concentrations in Drinking Water

Potential concentrations of thiophanate-methyl and carbendazim in drinking water sources were estimated using modelling results. Some monitoring data were available for carbendazim in the United States, but the paucity of the data did not allow for representative exposure estimates to be calculated for carbendazim in Canadian drinking water sources. Summary statistics from the assessment of modelling for thiophanate-methyl and carbendazim are presented in Appendix VIII (Tables 2 and 3, respectively). When available, monitoring data indicate concentrations known to exist in the environment but are unlikely to capture the peak concentrations because of the limited nature of sampling. Thus, monitoring data are generally considered a lower-bound estimate of the concentrations that may be expected in the environment. Modelling estimates are developed with a number of conservative assumptions and are generally considered upper-bound estimates. Further information on the estimation of concentrations in potential sources of drinking water is found in Appendix IX.

Drinking water modelling for thiophanate-methyl and carbendazim was conducted using the maximum foliar application rate. However, after the modelling was completed, further information on the use pattern indicates that the major uses are likely to be seed treatment and turf. Thus, the modelling will be revised concurrently with the revision of the dietary risk assessment, which will occur once the data requested in this PRVD are received. The modelling refinement will consider updated information on the use pattern including drift considerations, application rates, timing of application and regional scenarios.

3.4.3 Drinking Water Exposure and Risk Assessment

The acute and chronic EECs for thiophanate-methyl and carbendazim are summarized in Appendix VIII (Table 4). The acute and chronic EECs for thiophanate-methyl of 56 and 3.4 µg/L, respectively, are less than the respective DWLOCs, indicating that the combined exposure from food and water is acceptable. For carbendazim, the acute and chronic EEC of 33 and 11 µg/L, respectively, are less than the respective DWLOCs, indicating that the combined exposure from food and water is acceptable. The DWLOC for cancer includes potential exposure from both thiophanate-methyl and carbendazim. Therefore, it is appropriate to compare this to the combined chronic/cancer EEC of 12.9 µg/L, expressed in carbendazim equivalents. This exceeds the DWLOC. The potential cancer risk from drinking water exposure is uncertain, as EEC estimates are based on conservative upper bound assumptions from water modelling. Once further information on the use pattern is considered, exposure from drinking water will be reassessed.

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

Thiophanate-methyl is registered for residential gardens and golf courses. Therefore, an aggregate risk assessment would consider exposure from food, drinking water, and gardening or golfing. As the potential cancer risk from drinking water exposure is uncertain, an aggregate risk assessment combining exposure from food, drinking water and residential uses was not conducted at this time. As mentioned above, the drinking water estimates were based on modelled results and include a number of conservative assumptions. Upon receipt of data requested in this PRVD, updated use pattern information including drift considerations, application rates, timing of application and regional scenarios will be used to revise the drinking water estimates for the aggregate cancer risk assessment before making a regulatory decision. If refinements in the drinking water estimates are possible, a full aggregate assessment may be conducted at that time.

3.6 Incident Reports

Starting April 26, 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Incidents are classified into six major categories including effects on humans, effects on domestic animals and packaging failure. Incidents are further classified by severity, in the case of humans for instance, 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 will examine 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 will be taken, ranging from minor label changes to discontinuation of the product. Incident reports reflect the observations and opinion of the person reporting it and the Incident Reporting Program does not include validation of the reports. The PMRA collects incident reports in an effort to establish trends and the publishing of individual reports should not be considered as a statement of causality.

There were no incident reports submitted for thiophanate-methyl as of May 12, 2009.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

The fate and behaviour of thiophanate-methyl has been described in Re-evaluation Note REV2007-12, *Preliminary Risk and Value Assessments of Thiophanate-Methyl.* The data are summarized in Appendix X, Tables 1 to 4.

4.2 Effects on Non-target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants (Appendix X, Tables 5 to 6). Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (e.g. direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

The results of the risk assessment of the effects of thiophanate-methyl on terrestrial organisms is reported in Re-evaluation Note REV2007-12, *Preliminary Risk and Value Assessments of Thiophanate-Methyl*. During the consultation period for REV2007-12, the registrant proposed to lower the maximum application rate from 17.5 kg a.i./ha to 12.25 kg a.i./ha as used in turf.

The potential risk, based on the new proposed rate, was assessed and showed that foliar applications of thiophanate-methyl do not pose a risk to bees present in-field, except at the application rates used on turf (RQ 1.1) (Table 7, Appendix X). The risk to bees is negligible off-field (Table 9, Appendix X). During the consultation period, the registrant submitted data from two laboratory studies on effects on earthworms in artificial soil and results of two field studies on the impact on earthworms. The two field studies did not provide adequate information for a risk assessment. A two-week laboratory study indicated negligible acute and chronic risk to earthworms. However, a second laboratory study, with a duration of eight weeks, showed that thiophanate-methyl posed a risk, as the RQ exceeded the LOC at nearly all application rates with regard to earthworms present in-field. As a result, a refinement of the risk assessment was conducted taking into consideration the exposure concentrations of thiophanate-methyl that could be present in terrestrial habitat directly adjacent to the application field through drift of spray. Spray drift data for a fine ASAE droplet size, as is generally used in ground boom applications of herbicides, indicate that the maximum amount of spray that will drift one metre down wind from the point of application during spraying is 11%. The risk off-field based on exposure to 11% spray drift, was negligible, except mainly at the application rates used in turf (Table 9, Appendix X). Details are provided in Appendix I (Responses to Comments).

Details of the assessment of risk to birds is reported in Re-evaluation Note REV2007-12, *Preliminary Risk and Value Assessments of Thiophanate-Methyl.* The new proposed rate for use on turf (12.25 kg a.i./ha) was assessed and identified that there is acute and dietary risk to the American robin and Field sparrow, from spray applications at rates used for turf, when these birds are present in-field (Tables 8, Appendix X). The assessment was based on the conservative assumption that 100% of the diet is contaminated. However, given the mobile nature of birds the exposure would be less. The risk from spray applications is negligible when birds are present off-field (Table 10, Appendix X). With respect to reproductive effects in birds present in-field, the level of concern is not exceeded except at the application rates used on turf (Table 8, Appendix X). Off-field, the reproductive risk was negligible (Table 10, Appendix X). Granular applications of thiophanate-methyl which are used on turf, did not exceed the level of concern for acute risk, except for small birds the size of a sparrow. The threshold for risk on an area basis is 5.4 LD_{50}/m^2, which was exceeded by the field sparrow (9.2 LD_{50}/m^2).

Details of the assessment of risk to mammals is reported in Re-evaluation Note REV2007-12, *Preliminary Risk and Value Assessments of Thiophanate-Methyl.* The new proposed rate of 12.25 g a.i./ha as used in turf poses an acute risk to small mammals only when they are present in-field (Table 8, Appendix X). Acute risk to small mammals when they are exposed to lower application rates or when they are present off-field is negligible (Table 10, Appendix X). Thiophanate-methyl poses a dietary risk to small mammals present in-field (Table 8, Appendix X) and at a reduced level off-field (Table 10, Appendix X). The assessment of risk to small mammals present in-field was also based on the conservative assumption that 100% of the diet is contaminated.

4.2.2 Effects on Aquatic Organisms

Based on tests with *Daphnia magna,* a screening level assessment showed that exposure to thiophanate-methyl and the transformation product carbendazim is not of concern from acute toxicity to freshwater aquatic invertebrates, but there is risk from chronic toxicity from exposure to carbendazim,(Table 11, Appendix X). The chronic risk LOC is also exceeded when aquatic invertebrates are exposed to carbendazim that is present in water from both spray drift and runoff of thiophanate methyl (Tables 12 and 13, Appendix X). With regard to runoff, the risk of acute effects to freshwater invertebrates was assessed against the 90^{th} percentile of the peak concentrations of TPM. Since the duration of a chronic test for *Daphnia magna* is 21 days, the risk from chronic effects to freshwater fish is assessed against the 90^{th} percentile of the 21-d concentrations.

Based on tests with mysid shrimp, a screening level risk assessment showed that there is acute risk from exposure to thiophanate-methyl and chronic risk from exposure to carbendazim for estuarine/marine invertebrates,(Table 14, Appendix X). Refined risk assessment based on spray drift showed that there was negligible acute risk from thiophanate-methyl but there was chronic risk from carbendazim (Table 15, Appendix X). Refined risk assessment based on runoff showed that there was still acute risk from thiophanate-methyl and chronic risk from carbendazim (Table 16, Appendix X). The risk from acute effects to estuarine/marine invertebrates is assessed against the 90^{th} percentile of the peak concentrations of thiophanate-methyl in water. Since the duration of a chronic test for mysid shrimp is 14 days, the risk of chronic effects to estuarine/marine invertebrates is assessed against the 90^{th} percentile of the 21-d concentrations.

A screening level risk assessment showed that there was acute risk to fish from thiophanate-methyl but risk to the early life stage of the channel catfish from exposure to carbendazim following direct application of thiophanate-methyl showed negligible risk (Table 17, Appendix X). A refined risk assessment shows that exposure of thiophanate-methyl through spray drift or runoff poses negligible acute risk to fish as tested on rainbow trout and bluegill sunfish (Table 18 and 19, Appendix X). The risk from acute effects to freshwater fish was assessed against the 90^{th} percentile of the peak concentrations of TPM in water. The risk of sub-chronic effects (early life stage test) to freshwater fish was assessed against the 90^{th} percentile of the average of the yearly concentrations.

The risk to aquatic plants, algae and diatoms was based on toxicity of duckweed (*Lemna gibba*), green algae (*Kirchneria subcapitata*), freshwater diatom (*Navicula pelliculosa)* and marine diatom (*Skeletonema costatum*). The screening level risk assessment indicated negligible risk to *Lemna gibba* and identified a risk to the green alga and the freshwater and marine diatoms at the maximum application rate of 12.25 kg a.i./ha (Table 24, Appendix X). Refinement of the risk based on exposure to spray drift of 11% of the application rate and to exposure from runoff, showed negligible risk (Tables 25 and 26, Appendix X).

Tests on sheepshead minnow showed that thiophanate-methyl at the screening level, poses negligible acute risk to estuarine/marine fish (Table 20, Appendix X). There are no acute or chronic toxicity data available on the effects of the transformation product carbendazim on estuarine/marine fish.

Since no data on amphibians were available for thiophanate-methyl or the transformation product carbendazim, the most sensitive toxicity data for freshwater fish were used as a surrogate for assessment of the potential risk. A screening level assessment indicated an acute risk from thiophanate-methyl (Table 21, Appendix X). A refined risk assessment based on acute toxicity data and exposure to spray drift from 11% of the application rate showed that thiophanate-methyl posed some risk to amphibians as there was a slight exceedance of the LOC (RQ 1.08) (Table 22, Appendix X). Assessment of the risk of carbendazim to amphibians was based on early life stage toxicity data for channel catfish. A screening level assessment showed that there was risk (Table 21, Appendix X), but a refined risk assessment based on 11% spray drift of the parent compound showed negligible risk to amphibians from carbendazim, as the LOC was not exceeded (Table 22, Appendix X). The risk to amphibians from thiophanate-methyl and carbendazim in runoff was also negligible (Table 23, Appendix X).

5.0 Value

5.1 Commercial Class Products

5.1.1 Alternatives to Commercial Class uses of thiophanate-methyl

Appendix XI lists the registered chemical alternatives for the uses of thiophanate-methyl that the registrant continues to support but that had raised some concerns in the Preliminary Risk assessment (PRA) as a result of this re-evaluation. The PMRA has not commented on the availability and extent of use of these alternative pesticides. One or more alternative active ingredients are registered for most site-pest combinations, except for the use of thiophanate-methyl to control powdery mildew on raspberries, septoria leaf spot on aspen and poplars, and copper spot on turf. The PMRA has not received any comments in response to the publication of REV2007-12 concerning the importance of those uses for which there are no registered alternative active ingredients in Canada. On the contrary, many comments were received concerning some important uses of thiophanate-methyl, for which there are one or more registered alternatives. Nevertheless, thiophanate-methyl is an important component in the management of diseases on these sites and contributes to sustainability and integrated pest management. In particular, many stakeholders in their comments have emphasized thiophanate-methyl's role in fungicide rotation for preventing or delaying the development of fungicide resistance, especially on sites where only a few alternatives are registered and concerns have been raised about the development of fungicide resistance. The PMRA response to these comments is provided in Appendix I.

Most non-chemical alternatives are focussed on general cultural practices (including reducing initial inoculum by destroying infected plant material, weed control since they can harbor disease, crop rotation, resistant varieties, appropriate soil cultivation and modification of habitat to minimize environmental factors that may favour disease development or spread). The PMRA searched for information available for specific site-pest combinations and found a number of non-chemical pest control measures that are summarized in Appendix XI. The effectiveness and extent of use of these non-chemical control measures have not been verified. The PMRA has not received any specific comments concerning non-chemical alternatives in response to REV2007-12. Most responses from grower groups pertaining to some important uses have indicated that thiophanate-methyl, although a critical component of their pest management systems, is not the single disease management method they rely upon. Rather, they use this fungicide along with other traditional and new non-chemical pest management practices in an Integrated Pest Management (IPM) program.

The concerns raised about widespread resistance to thiabendazole, another group 1 fungicide, cross resistance to thiophanate-methyl, and recent recommendations from some resistance management experts, have led the PMRA to propose a generic label wording upgrade (see Section 8.1.3) to strengthen the voluntary resistance management portion of thiophanate-methyl labels targeted to the potato seed piece treatment sector. Since pest management is in constant evolution, the PMRA strongly encourages users of thiophanate-methyl products to regularly consult other sources of information such as their extension specialists, industry association publications and governmental web sites to ensure the sustainability and adequacy of their pest management options.

5.2 Domestic Class Products

All Domestic Class uses of thiophanate-methyl are supported by the registrant and are listed in Appendix IVb. The PMRA has no information about the extent of use of the single thiophanate-methyl Domestic Class product.

5.2.1 Alternatives to Domestic Class Products

The single end use Domestic Class product is co-formulated with two insecticide active ingredients and another fungicide, all of which are currently under re-evaluation. There exist several registered alternative active ingredients for all of the fungicidal uses listed on the label for this product. The PMRA has not received any specific comments concerning the value of the Domestic Class uses of thiophanate-methyl in response to REV2007-12.

5.3 Value of Thiophanate-methyl

Thiophanate-methyl and other benzimidazole fungicides have been used extensively in Canada. However, over-reliance on this family of fungicides has resulted in the development of fungicide resistance on many combinations of sites and pests in some areas of the country. Although several alternative active ingredients and new chemistries are now available for many of the site-pest combinations on the thiophanate-methyl labels, this active ingredient still plays a role in resistance management in areas of the country where benzimidazole resistance is not present, by allowing rotation with the use of these new fungicides. Resistance management and fungicide rotation are important especially for sites that have only a few registered alternative fungicides such as greenhouse ornamentals and seed treatments.

In this refined risk and value assessment, the site-pest combinations for which thiophanate-methyl is the only registered pesticide have been identified. There are no alternative registered active ingredients in Canada for the following site-pest combinations:

- Septoria leaf spot on aspen and poplars
- Powdery mildew on raspberries
- Copper spot on turfgrass

These uses, however, are very small and the PMRA has not received any comments from stakeholders and the public concerning their importance.

Although there exist some registered alternative active ingredients, thiophanate-methyl is also of economic value for some other uses where risk issues have been raised:

- Potato seed piece treatment (seed treatment); despite the availability of alternative active ingredients, thiophanate-methyl is still the preferred active ingredient for this use in many large Canadian potato growing areas. The PMRA has received several comments and letters of support from potato seed grower groups about the importance of thiophanate-methyl for their sector. The PMRA has addressed these comments in Appendix I.

- Dry common beans (seed treatment); despite the availability of alternative active ingredients, thiophanate-methyl is still the preferred active ingredient for this use in many large Canadian bean growing areas. The PMRA has received several comments from seed grower groups about the importance of thiophanate-methyl to their sector. The PMRA has addressed these comments in Appendix I.

- Turf; despite the availability of alternative turf fungicides to control various fungal pests on this site, thiophanate-methyl is preferred for some uses. Some golf course superintendents have a preference for a fertilizer-fungicide granular product that contains thiophanate-methyl over alternative turf fungicides. This product is registered in Canada under the *Fertilizers Act*.

- Greenhouse potted ornamentals; despite the availability of alternative fungicides, this industry, because of its small cultivated area, lacks alternative new products. Nevertheless, growers produce high value crops that require a very high standard of phytosanitary quality, especially for export. Despite the small size of this industry in terms of cultivated area and pesticide market, it constitutes significant economic activity in Canadian agri-business and the economy of some Canadian provinces. The impact of the potential loss of the use of thiophanate-methyl on this site is unknown at this time.

The value of the Canadian horticulture industry is estimated at around $5 billion annually at the farm gate level. In 2005, floriculture and nursery farm gate sales alone accounted for $1.9 billion or approximately 37% of all horticultural sales. This is without taking into account the impact of this industry upstream and downstream of the horticultural production chain, on employment, economic activity, and sales and income taxes to the two levels of governments and to municipalities.

6.0 Pest Control Product Policy Considerations

6.1 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, when they meet the TSMP policy criteria.

During the review process, thiophanate-methyl 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*. Substances associated with the use of thiophanate-methyl were also considered, including transformation products formed in the environment, and contaminants and formulants in the technical product and the end-use product. Thiophanate-methyl and its transformation products were 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 Kow ≥5 or BCF ≥5000 (or BAF ≥5000). In order for thiophanate-methyl 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 and end-use product, including formulants, were 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:

Thiophanate-methyl does not meet Track 1 criteria. Thiophanate-methyl does not meet the Track 1 criterion for persistence, as its half-life values in water/sediment (< 1 day), and soil (< 1 day) are below the Track 1 criteria. Thiophanate-methyl 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 (1.3×10^{-5} Pa) and Henry's Law constant ($K=2.69 \times 10^{-7}$ atm m^3 mol). Thiophanate-methyl does not meet the Track 1 criterion for bioaccumulation, as its octanol-water partition coefficient (log K_{ow} 1.38) is below the Track 1 criterion. Therefore, thiophanate-methyl does not meet the Track 1 criteria, and is not considered a Track 1 substance.

Thiophanate-methyl does not form any transformation products that meet the Track 1 criteria.

There are no Track 1 contaminants in the technical products or end use products.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, formulants and contaminants in the technical and end-use products are assessed against the formulants and 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*. This list of formulants and contaminants of health and environmental concern are identified using existing policies and regulations including: the federal Toxic Substances Management Policy; the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol); and the PMRA Formulants Policy as described in the PMRA Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*. The *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* is maintained and used as described in the PMRA Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

The *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* consists of three parts:

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.

The contaminants to which Part 3 applies meet the federal Toxic Substances Management Policy criteria as Track 1 substances, and are considered in section 6.1. The following assessment refers to the formulants and contaminants in Part 1 and Part 2 of the list.

Technical grade thiophanate-methyl and the end-use products do not contain any formulants or contaminants of health or environmental concern 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*.

7.0 Summary

7.1 Human Health and Safety

The toxicology database for both thiophanate-methyl and carbendazim require confirmatory data for the risk assessment and/or use expansion. In short and long-term animal toxicity studies, the liver was the primary target for both compounds. Both thiophanate-methyl and carbendazim induced liver tumours in male and female mice. Thiophanate-methyl also induced thyroid tumours in male rats and ovarian granulosa cell tumours and leuteomas were noted in one strain of mice treated with carbendazim. Carbendazim and thiophante-methyl were not mutagenic but are well known aneugens. However, a metabolite common to carbendazim and thiophante-methyl was mutagenic and in addition thiophante-methyl and some of its metabolites share a thioureas moiety that is implicated in thyroid tumor formation. Thiophanate-methyl produced additional effects in the thyroid and kidney, and carbendazim also induced testicular toxicity. For thiophanate-methyl, potential clinical signs for neurotoxicity were noted in both the 1-year dog study and the two-generation reproduction study. Thiophanate-methyl may have anti-thyroid activity. As well, thiophanate-methyl rapidly metabolises to carbendazim, which induces severe central nervous system (CNS) and craniofacial malformations in rats in the absence of maternal toxicity, as well as in hamsters at maternally toxic doses. The risk assessments for both thiophanate-methyl and carbendazim protect against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

7.1.1 Occupational Risk

Non-cancer and cancer risk estimates associated with mixing, loading and applying activities for most proposed agricultural label uses are not of concern, provided engineering controls, personal protective equipment, and additional mitigation measures as listed in Section 8 are implemented.

Worker risk estimates for commercial seed treatment for dry common beans and sweet corn are of concern and these uses need further investigation of the use through exposure studies or consideration of removal of that use.

Worker risk estimates for potato seed piece treatment is of concern and data is requested for treatment and planting.

Postapplication risks for workers were not of concern when the proposed mitigation measures are applied. However, a number of proposed REIs may not be considered agronomically feasible.

7.1.2 Dietary Risk from Food

Acute, chronic and cancer dietary risk from food-only exposure to both thiophanate-methyl and carbendazim are not of concern for all sub-populations.

7.1.3 Dietary Risk from Drinking Water

- Acute and chronic EECs for thiophanate-methyl are not of concern for all sub-populations.
- Acute and chronic EECs for carbendazim are not of concern for all sub-populations.
- EEC for cancer from both thiophanate-methyl and carbendazim exceeds the DWLOC. The potential cancer risk from drinking water exposure is uncertain, as EEC estimates are based on conservative upper bound assumptions from water modelling. Once further information on the use pattern is considered, exposure from drinking water will be reassessed.

7.1.4 Residential Risk

Non-cancer risks to applicators are not of concern for residential use. Cancer risk to residential applicators is not of concern if the proposed label limitation of 3 applications per year is followed for the domestic product.

Non-occupational postapplication risk is not of concern for gardeners and golfers, provided the application rate for golf course turf is reduced.

7.1.5 Aggregate Risk

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

Thiophanate-methyl is registered for residential gardens and golf courses. Therefore, an aggregate risk assessment would consider exposure from food, drinking water, and gardening or golfing. As the potential cancer risk from drinking water exposure is uncertain, an aggregate risk assessment combining exposure from food, drinking water and residential uses was not conducted at this time.

7.2 Environmental Risk

Thiophanate-methyl is nonpersistent in the terrestrial and aquatic environments as it transforms rapidly to carbendazim. The latter is moderately persistent in soils and moderately persistent to persistent in aquatic environments. Carbendazim adsorbs to soil and hence is only slightly mobile in soil. The risk from thiophanate-methyl to birds and mammals is negligible, given their mobile nature, and hence, reduced exposure. Thiophanate-methyl does not present a risk to aquatic organisms, except for a slight risk to amphibians. The transformation product, methyl 2-benzimidzolylcarbamate (carbendazim) poses some chronic risk to aquatic invertebrates. Additional risk reduction measures need to be observed.

7.3 Value

Important fully registered uses of thiophanate-methyl include seed treatment of dry common beans for the control of seedborne anthrachnose, potato seed treatment for the control of several seed-borne and soil-borne diseases, turf treatments for the control of several fungal diseases, and drench and foliar treatments of greenhouse potted ornamentals for the control of several soil-borne and foliar plant diseases of ornamentals.

Several alternative active ingredients and new chemistries are now available for many site-pest combinations. Thiophanate-methyl plays a role in the integrated management of many important diseases where there are few comparable alternatives. Thiophanate-methyl contributes to pest management and sustainability, since it plays a role in resistance management in areas of the country where benzimidazole resistance is not present, by allowing rotation with the use of these new fungicides on some sites. Resistance management and fungicide rotation are important especially for sites that have only a few registered alternative fungicides such as greenhouse ornamentals and seed treatments.

8.0 Proposed Regulatory Decision

8.1 Proposed Regulatory Actions

8.1.1 Proposed Regulatory Action Related to Human Health

8.1.1.1 Proposed Mitigation for Mixer, Loader, Applicator and Bystander Exposure

Most of the mitigation measures below have been proposed by the registrant and/or growers as a result of comments from the REV2007-12.

Domestic Product:
The dust formulation for roses, ornamentals and junipers must be limited to 3 applications per year to mitigate cancer concerns. The following statement should be added to the domestic label:

"Limit of 3 applications per year."

Label clarifications:
To mitigate potential risk concerns for postapplication workers and drinking water, it is recommended that all label directions concerning the application of thiophanate-methyl on turf have the following statement:

"Turf use is for golf course greens and tees only."

To avoid possible confusion regarding thiophanate-methyl use on roses, the label directions concerning the application of thiophanate-methyl on outdoor roses should have the following statement:

"Not for use on greenhouse roses."

Wettable Powder in Water Soluble Packaging (WSP):
All thiophanate-methyl products currently listed as wettable powders must be in water soluble packaging (except for those intended for seed treatment use). Label language should be clarified to indicate directions for water soluble packaging.

Number of applications:
The maximum number of applications for all registered commodities must be two per crop (with the exceptions of turf (where 2 applications can be made at the lower rates plus one at the high rate at the end of the season) and on-farm seed treatment (one application). For all uses, the interval of application will be a minimum of 7 days. It is therefore necessary to change the label for all crops accordingly.

Rate reduction:
The maximum rate for turf (use on golf course greens and tees only) must be lowered to 12.25 kg a.i./day. At this high rate, only 1 application per year is allowable. This application is to occur at the end of the golf season.

Use Precautions:
There may be potential for exposure to bystanders from drift following pesticide application to agricultural areas. In the interest of promoting best management practices and to minimize human exposure from spray drift or from spray residues resulting from drift, the following label statement is required:

"Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

Engineering Controls and Personal Protective Equipment:
Statements must be amended (or added) to include the following directions to the appropriate labels in order to mitigate the risk of exposure to thiophanate-methyl:

<u>Mixing/Loading/Applying:</u>
The following crops require coveralls over long sleeves and long pants and chemical resistant gloves for mixing, loading and applying:

- Aspen and Poplar
- Apples and pears
- Lowbush blueberries
- Cherries, nectarines, plums, prunes and peaches
- Raspberries
- Strawberries
- Sugar beets
- White beans (see additional mitigation below)
- Outdoor ornamentals and roses (see additional mitigation below)
- Golf courses tees and greens (turf)
- Greenhouse potted ornamentals (see additional mitigation below)
- Dry common beans (on farm seed treatment) (see additional mitigation below)
- Sweet corn (on farm seed treatment) (see additional mitigation below)
- Potatoes (cut seed treatment) (see additional mitigation below)

<u>Additional Mixing/Loading/Applying Mitigation</u>:
White beans:

- Groundboom: Limit the amount of kg a.i. handled per person per day to 315 kg a.i. (area treated per day of 200 ha at maximum rate) for all groundboom applications.
- Groundboom open cab: mixers/loaders and applicators must wear chemical resistant coveralls over a single layer (long pants and long sleeved shirt), gloves and respirator.

Outdoor ornamentals and roses:

- Handheld equipment: Limit the amount of kg a.i. handled per person per day to 1 kg a.i. and wear maximum PPE (chemical resistant coveralls over single layer (long pants and long sleeved shirt), gloves and a respirator).
- Airblast requires closed cab with single layer PPE (long pants and long sleeved shirt) or open cab with maximum PPE (chemical resistant coveralls over single layer (long pants and long sleeved shirt), gloves and a respirator) including chemical resistant headgear. Workers mixing and loading require coveralls over single layer (long pants and long sleeved shirt).

Greenhouse potted ornamentals:

- Hand held equipment: Limit the amount of kg a.i. handled per person per day to 1 kg a.i. and wear maximum PPE (chemical resistant coveralls over single layer (long pants and long sleeved shirt), gloves with a respirator). NOTE: this foliar use requires a 20 day REI, which may not be feasible.
- Drench application must not have contact with foliage, otherwise it must adhere to the 20 day REI.

Dry common beans (on farm seed treatment):

- A dust mask is required in addition to the PPE listed previously.
- Amount treated per person per day is limited to 3000 kg (to account for potential exposure when planting treated seed). A planting study is also required. The registrant had proposed looking at the Agricultural Handler Exposure Task Force (AHETF) data to fill this data gap. This data is pending review.

Sweet corn (on farm seed treatment):

- A dust mask is required in addition to the PPE listed previously.

Potatoes (on farm cut seed treatment):

- A dust mask is required in addition to the PPE listed previously.
- Amount treated per person per day is limited to 10 000 kg of cut potato seed.

Restricted-entry Intervals:
The restricted-entry intervals listed below are proposed to be added to the appropriate labels.

Table 8.1.1.1 Recommended Restricted-entry Intervals

Activity	Proposed REI (days)
Lowbush Blueberries (0.77 kg a.i./ha)	
all activities	1
Raspberries (0.77 kg a.i./ha)	
all activities	1
Strawberries (0.77 kg a.i./ha)	
all activities	1
White Beans (1.58 kg a.i./ha)	
hand weed	12hr
irrigate, scout	2
hand harvest	3
Sugar beets (0.39 kg a.i./ha)	
all activities	12 hr
Apples and Pears (1.58 kg a.i./ha - Western)	
hand weed, hand prop, hand prune, hand pinch, hand tie, hand train	12hr
hand harvest	5
hand thin	9
scout	11
Apples and Pears (0.4375 kg a.i./ha - Eastern)	
hand weed, hand prop, hand prune, hand pinch, hand tie, hand train, hand harvest	12hr
hand thin	2
scout	4
Peaches, Nectarines, Plums, Prunes and Cherries (1.23 kg a.i./ha)	
hand weed, hand prop, hand prune, hand pinch, hand tie, hand train	12hr
hand harvest	4
hand thin	8
scout	9

Activity	Proposed REI (days)
Aspen and Poplar (0.77 kg a.i./ha)	
all activities	12hr
Roses and Ornamental Plants Outdoor (0.525 kg a.i./ha)	
All activities (excluding cut flowers)	2
cut roses	5
Greenhouse Potted Ornamentals (0.595 kg a.i./ha)	
All activities for potted ornamentals (regular application methods)	20 (not feasible)
All activities for potted ornamentals (drench application) NO TPM contact with the foliage during application	12 hr
Turf	
mowing	1
All other worker activities	12 hr

Commercial Seed Treatment:
Health risk concerns have been identified for workers in commercial seed treatment facilities using thiophanate-methyl to treat dry common beans and seed corn, even after consideration of more feasible engineering controls and PPE. Further investigation of the use through exposure studies, or removal of these uses need to be considered.

8.1.1.2 Residue Definition for Risk Assessment and Enforcement

The nature of the thiophanate-methyl residue is defined as the sum of thiophanate-methyl and carbendazim, expressed as carbendazim. Maximum residue limits (MRLs) for residues in or on food commodities are currently expressed in terms of benomyl, carbendazim and thiophanate-methyl expressed as carbendazim under the *Pest Controls Products Act*. For the estimation of dietary risk, the residue is defined as the sum of thiophanate-methyl, carbendazim and 2-amine-1-H-benzimidazole, expressed as carbendazim.

8.1.1.3 Maximum Residue Limits for Thiophanate-methyl in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian maximum residue limits and to remove MRLs that are no longer supported. The MRLs for thiophanate-methyl were not re-evaluated. The PMRA recognizes, however, that interested parties may want to retain an MRL in the absence of a Canadian registration to allow legal importation of treated commodities into Canada. The PMRA requires similar chemistry and toxicology data for such import MRLs as those required to support Canadian food use registrations. In addition, the Agency requires residue data that are representative of use conditions in exporting countries, in the same manner that representative residue data are required to support domestic use of the pesticide. These requirements are necessary so that the PMRA may determine whether the requested MRLs are needed and to ensure they would not result in unacceptable health risks.

After the revocation of an MRL or where no specific MRL for a pest control product has been established in the Food and Drug Regulations, subsection B.15.002(1) applies. This requires that residues, for foods which do not have MRLs specified, do not exceed 0.1 ppm and has been considered a general MRL for enforcement purposes. However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*.

As indicated in Table 8.1.1.4, the *Pest Control Products Act* specifies MRLs for thiophanate-methyl residues in apples, apricots, beans, blackberries, boysenberries, carrots, cherries, citrus fruits, cucumbers, grapes, melons, mushrooms, peaches/nectarines, pears, pineapples (edible pulp), plums, pumpkins, raspberries, squash, strawberries and tomatoes. Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specified MRL, must not exceed the general MRL of 0.1 ppm.

Table 8.1.1.4 Maximum residue limits for Benomyl, Carbendazim and Thiophanate-methyl in Canada*

Commodity	Canadian MRL for Thiophanate-methyl, ppm
Apples	5
Apricots	5
Beans	1
Blackberries	6
Boysenberries	6
Carrots	5
Cherries	5
Citrus fruits	10
Cucumbers	0.5
Grapes	5
Melons	0.5
Mushrooms	5
peaches/nectarines	10
Pears	5
Pineapples (edible pulp)	1
Plums	5

Commodity	Canadian MRL for Thiophanate-methyl, ppm
Pumpkins	0.5
Raspberries	6
Squash	0.5
Strawberries	5
Tomatoes	2.5

* The residue definition is methyl 1-(butylcarbamoyl)benzimidazol-2-ylcarbamate (benomyl), methyl benzimidazol-2-ylcarbamate (carbendazim) and 1,2-di-(3-methoxy-carbonyl-2-thioureido)benzene (thiophanate-methyl), expressed as carbendazim

8.1.2 Proposed Regulatory Action Related to Environment

The risk assessment has indicated that adverse effects on non-target aquatic organisms are expected. To reduce the effects of thiophanate-methyl and its transformation product carbendazim in the environment, mitigation in the form of precautionary label statements and buffer zones are required. Environmental mitigation statements are listed below (*Label Amendments for Commercial Class Products Containing Thiophanate-methyl*).

Proposed Label Amendments for Products Containing Thiophanate-methyl

Add to ENVIRONMENTAL HAZARDS:

The labels of all products should be amended to include the following statements:

- TOXIC to birds and small wild mammals.
- TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.
- To reduce runoff from treated areas into aquatic habitats avoid application to areas with a moderate to steep slope, compacted soil, or clay.
- Avoid application when heavy rain is forecast.
- Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.
- The use of this chemical may result in contamination of groundwater particularly in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow

For seed treatment products the labels should be amended to include the following additional statements:

- Treated seed is toxic to birds.

- Treated seed is toxic to small wild mammals.

- The following statement must appear on the seed package or on a conspicuous label attached to the package:

- TOXIC to birds. Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned-up from the soil surface.

- TOXIC to small wild mammals. Any spilled or exposed seeds must be incorporated into the soil or otherwise cleaned-up from the soil surface.

Add to DIRECTIONS FOR USE

The following statement is required for all domestic pesticide products. The statement is not required on ready-to-use domestic products.

- To minimize possible contamination of groundwater, the use of spot treatment applications is recommended in areas where soils are permeable (e.g. sandy soil) and/or the depth to the water table is shallow.

- **DO NOT** apply to any body of water.

- Avoid application of this product when winds are gusty.

The following statement is required for all pesticide products (agricultural, commercial, or domestic):

- **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.

The following statement is required for all broadcast pesticide products (agricultural or, commercial). The statement is not required on ready-to-use domestic products.

- **DO NOT** apply this product directly to freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands), estuarine/ marine habitats.

The following statement is required on all agricultural or commercial products, unless aerial application (blueberries, white beans) is permitted:

- **DO NOT** apply by air.

- 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.

- Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

- Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. To reduce drift caused by turbulent wingtip vortices, the nozzle distribution along the spray boom length **MUST NOT** exceed 65% of the wing- or rotorspan.

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 freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Table 1 Buffer Zones For the Protection of Aquatic Life

Method of application	Crop	Buffer Zones (metres) Required for the Protection of:			
		Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:	
		Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
Field sprayer*	Sugar beets, blueberries, raspberries, strawberries, white beans, aspen, poplar	2	1	1	1
	Turf (reduced maximum rate of 12.25 kg a.i./ha proposed by registrant)	5	3	1	1

Method of application	Crop		Buffer Zones (metres) Required for the Protection of:			
			Freshwater Habitat of Depths:		Estuarine/Marine Habitats of Depths:	
			Less than 1 m	Greater than 1 m	Less than 1 m	Greater than 1 m
Airblast	Aspen, poplar	Early growth stage	20	15	3	1
	Peaches, nectarines, plums, prunes, cherries	Early growth stage	25	15	4	1
	Apples, pears	Late growth stage	15	10	3	1
Aerial	Blueberries	Fixed	15	10	1	1
		Rotary wing	15	5	1	1
	White beans	Fixed	35	15	1	1
		Rotary wing	30	10	1	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.

8.1.3 Proposed Regulatory Action Related to Value

The following regulatory actions regarding value are proposed for the continued registration of thiophanate-methyl:

- The PMRA is recommending that the voluntary resistance management labelling of thiophanate-methyl be strengthened to current standards. In particular the PMRA is proposing that the labels for potato seed-piece treatment products containing thiophanate-methyl, among other standard resistance management labelling, include the statement:

> "Do not use [end-use product name] or other Group 1 fungicide in any two consecutive seed generations. If potatoes were treated with MERTECT SC Fungicide or another group 1 fungicide prior to storage in the preceding fall, do not use [end-use product name] or any other product containing thiophanate-methyl at planting."

The labels for all end-use products containing thiophanate-methyl that cannot be packaged as WSB should be amended to reflect currently supported uses (including other label amendments resulting from the risk assessments) following publication of the PMRA's RVD.

8.2 Additional Data Requirements

8.2.1 Data Requirements Related to Toxicology

Thiophanate-methyl
Potential clinical signs of neurotoxicity (tremors/convulsions) were noted in a 1-year oral dog study with thiophanate-methyl, and in a two-generation reproduction study in which post-weanling male pups showed reduced performance in an open-field test. Thiophanate-methyl may also have direct antithyroid activity. Thyroid hormones are critical for the development of mammalian fetal and neonatal brain. A deficiency of thyroid hormones at an early developmental stage can lead to mental retardation and stunted growth. As well, thiophanate-methyl rapidly metabolises to carbendazim, which induces severe central nervous system and craniofacial malformations.

Uncertainty factors have been applied to account for the uncertainties and data gaps in the toxicity data base. Although the registrant has supplied acute and short-term neurotoxicity studies requested in REV2007-12, the following confirmatory data remain outstanding and are required to refine the risk assessment. In addition, any other studies conducted in response to the EPA 2001 RED should also be submitted to the PMRA.

- Developmental neurotoxicity in rats (DACO 4.5.14)
- Repeat-dose inhalation study (DACO 4.3.6 or 4.3.7)

Carbendazim
Carbendazim induces severe CNS and craniofacial malformations in rats in the absence of maternal toxicity, as well as in hamsters at maternally toxic doses. Uncertainty factors have been applied to account for the uncertainties and data gaps in the toxicity data base. Although not critical to the current TPM re-evaluation, the following data may be required to support any expansion of carbendazim use. Any other studies conducted in response to the EPA 2001 RED should also be submitted to the PMRA.

- Developmental neurotoxicity in rats (DACO 4.5.14)

8.2.2 Data Requirements Related to Occupational Exposure Assessment

8.2.2.1 Data required for continued registration

DACO 5.4/5.5	Mixer/loader/applicator - passive dosimetry data or biological monitoring data for on-farm potato seed treatment and planting.
DACO 5.4/5.5	Mixer/loader/applicator - passive dosimetry data or biological monitoring data for dry common beans and sweet corn on-farm planting. Data from the Agricultural Handler Exposure Task Force (AHETF) may fill this data gap.
DACO 5.4/5.5	Mixer/loader/applicator - passive dosimetry data or biological monitoring data for commercial seed treatment (dry common beans and sweet corn). Data from the AHETF may fill this data gap.

8.2.2.2 Data required for future use (for refinement only)

DACO 5.8	*In vivo* dermal absorption study*

* The registrant has submitted an *in vitro* study. However, the method did not meet the PMRA's needs for refinement.

8.2.3 Data Requirements Related to Dietary Exposure

Additional studies for thiophanate-methyl are required to confirm the dietary assessments and conclusions.

8.2.3.1 Data required for continued registration

DACO 7.2.2	Enforcement Analytical Methodology for plant and animal matrices (not required if a valid multi-residue analytical methodology is submitted)*
DACO 7.2.3	Inter-laboratory Analytical Methodology Validation
DACO 7.2.4	Multi-residue Analytical Methodology Evaluation

*The registrant has submitted an enforcement analytical method. However, the method does not comply with the Regulatory Directive DIR98-02 *Residue Chemistry Guidelines* (e.g. recovery information). Therefore this data requirement is still outstanding.

8.2.4 Data Requirements Related to Value

The PMRA does not have any specific data requirements relating to value at this time. Should the need arise to perform a social and economic value assessment for some uses that are proposed for deregistration, the PMRA will inform stakeholders of future data requirements relating to value.

The PMRA is seeking information on the availability and viability of alternative chemical and non-chemical pest management practices for the site and pest combinations registered for TPM. This information will allow the PMRA to refine sustainable pest management options for TPM.

The PMRA is soliciting information on the feasability of the proposed mitigation measures.

8.3 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03 and DACO tables, can be found on the Pesticides and Pest Management portion of Health Canada’s website at healthcanada.gc.ca/pmra. 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/toxiques-toxics/.

List of Abbreviations

°C	degree(s) Celsius
ADI	acceptable daily intake
a.i.	active ingredient
amu	atomic mass units
aPAD	acute population adjusted dose
ARfD	acute reference dose
BC	British Columbia
bw	body weight
BWI	body weight (fresh weight) of an individual [kg bw/ind]
CFIA	Canadian Food Inspection Agency
cm	centimetre(s)
cPAD	chronic population adjusted dose
d	day(s)
DACO	data code
DFR	Dislodgeable Foliar Residue
DI	dietary intake (per individual and day) = (EEC × FC) [mg a.i./ind/d]
DU	Dust or powder
dw	dry weight of diet [kg dw]
EC	emulsifiable concentrate
EC_{25}	concentration effective against 25% of test organisms [mg a.i./kg diet or mg a.i./L]
EC_{50}	median effective concentration [mg a.i./kg diet or mg a.i./L]
EEC	expected environmental concentration [also estimated environmental concentration]
FQPA	*Food Quality Protection Act*
FCR	feed consumption rate (per individual and day) [kg dw/ind/d]
FRAC	Fungicide Resistance Action Committee
fw	fresh-weight of diet [kg fw]
g	gram(s)
h	hour(s)
ha	hectare(s)
IPM	Integrated Pest Management
kg	kilogram(s)
K_d	Freundlich adsorption coefficient (a.k.a. soil sorption coefficient; soil-water partition coefficient [mL/g or complex]
K_{oc}	organic carbon adsorption coefficient (a.k.a. organic carbon partition coefficient; soil sorption constant) [mL/g or complex]
K_{ow}	*n*-octanol–water partition coefficient
km	kilometre(s)
LC_{50}	median lethal concentration [mg a.i./kg diet or mg a.i./L]
LD_{50}	median lethal dose [mg a.i./kg bw]
LOC	level of concern (RQ = 1)
LOEC	lowest observable effect concentration [mg a.i./kg diet or mg a.i./L]
LOEL	lowest observable dose level [mg a.i./kg bw]

m	metre(s)
m^3	metre(s) cubed
MB	Manitoba
mg	milligram(s)
MOE	margin of exposure
mol	mole
MRL	maximum residue limit
N/A	not available
NB	New Brunswick
NIOSH	National Institute of Occupational Safety and Health
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NS	Nova Scotia
ON	Ontario
Pa	Pascal(s)
PCP #	Registration Number under the Pest Control Products Act
PCPA	*Pest Control Products Act*
PE	Prince Edward Island
PHED	Pesticide Handlers Exposure Database
p*K*a	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
ppb	parts per billion
PPE	personal protective equipment
ppm	parts per million
PRA	Preliminary Risk Assessment
QC	Québec
RED	Reregistration Eligibility Decision
RQ	risk quotient
SF	safety factor
TC	transfer coefficient
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
URMULE	User Requested Minor Use Label Expansion
USC	Use Site Category
USEPA	United States Environmental Protection Agency
UF	uncertainty factor
US	United States
WP	Wettable Powder
WSB	Water Soluble Bag

Appendix I Comments and Response to REV2007-12

Comments Pertaining to Toxicology:

Comment: General comments concerning the use of safety factors for "severity of endpoint" and database deficiencies.

PMRA's Response: The uncertainty/safety factors (UF/SF) applied in the REV note reflect the PMRA's current standards for risk assessment. Additional UF/SF were added to the Thiophanate-Methyl (TPM)/Carbendazim risk assessments because of thyroid effects in the mouse, rat and dog (TPM), for the lack of developmental neurotoxicity studies for both compounds and for sensitivity of the young and severity of sperm effects for carbendazim. Pending any potential policy changes and the submission and evaluation of **all** data requirements, the UF/SFs in the TPM and Carbendazim assessments will be retained.

Comment: The EPA has placed a "reserve" on the repeat-dose inhalation study for TPM, pending the results from worker exposure studies (for greenhouse uses).

PMRA's Response: The PMRA concurs with the EPA and will place this data requirement, "on reserve".

Comment: The EPA did not request a repeat-dose inhalation study for Carbendazim. The registrant asks if this study will be required if the other toxicology studies for TPM and Carbendazim are conducted?

PMRA's Response: For the current use pattern, the PMRA will waive this data request. However, should the use pattern change, the PMRA retains the right to ask for a repeat-dose inhalation study with Carbendazim. The REV note will be adjusted accordingly.

Comment: The acute and chronic neurotoxicity studies have been submitted to the PMRA for review.

PMRA's Response: The PMRA acknowledges receipt of studies and currently has them under review.

Comment: The developmental neurotoxicity study for TPM was placed on reserve by the EPA, pending the review of the neurotoxicity studies. The registrants submitted a waiver request, claiming that there was no sensitivity difference between dams and pups to TPM in relation to measurements of thyroidal hormone levels and histopathological examination. Thus, a DNT study for TPM is not required.

PMRA Response: The PMRA requires a DNT study regardless of the outcome of the acute and subchronic neurotoxicity studies. The database shows decrements in circulating thyroid hormones in rats, mice and dogs. As stated in the PMRA REV Note, "Adequate circulating levels of thyroid hormones are critical for normal development of the mammalian fetal and neonatal brain...". In other words, the maternal circulating hormones have to be adequate for fetal and neonatal brain development. Subtle neurological effects are not evident in a standard developmental study. Furthermore, following the review of the neurotoxcity studies, the EPA is currently requiring a DNT study for TPM (letter to TPM Task Force, November 5, 2007). The EPA's letter predates Nisso America's waiver request to the PMRA (December 27, 2007).

Comment: The registrant cannot verify Cancer Q1* value in Table 1. The value is different when compared to the value in the EPA RED for Thiophanate Methyl:
PMRA: Cancer Q1* = 1.32×10^{-2}
EPA: Cancer Q1* = 1.16×10^{-2}
The registrant welcomes a discussion with the PMRA to discern these discrepancies between the agencies.

PMRA Response: The Unit risks are different because the EPA did not apply an allometric scaling adjustment factor. The PMRA will retain the use of the scaling adjustment factor and the Unit risk of 1.32×10^{-2}.

Comment: The registrant cannot verify the values in the Table 2 for Carbendazim. The values differ when compared to those of the EPA RED.

1. PMRA: Chronic dietary NOAEL = 9 mg/kg/day based on 2 year dog study with MBC (the abbreviation used for carbendazim by USEPA)
   EPA: Chronic dietary NOAEL = 2.5 mg/kg/day based on 2 year dog study with MBC (the abbreviation used for carbendazim by USEPA)

PMRA Response: The EPA used a NOAEL from a wettable powder formulation study (72.2 or 53% TGAI). The PMRA used a NOAEL of 9 mg/kg bw/d based on a technical grade active ingredient (TGAI) study, in which the compound had a purity of 99%.

2. PMRA: Cancer Q1* = 1.6×10^{-2}
   EPA: Cancer Q1* = 2.39×10^{-3}

PMRA Response: The Unit risks are different because the EPA did not apply an allometric scaling adjustment factor. The PMRA will retain the use of the scaling adjustment factor and the Unit risk of 1.6×10^{-2}.

Comments Pertaining to Occupational / Residential Exposure:

Comment: Nisso proposes to phase out the loose wettable powder product and replace it with a wettable powder sold only in water soluble bags. This change would include all uses with the exceptions of the use on mushrooms and the use on seed treatments.

PMRA's Response: The exposure assessment has been updated to reflect the use of water soluble bags for the following crops: greenhouse potted ornamentals, apples, pears, lowbush blueberries, peaches, nectarines, plums, prunes, cherries, raspberries, strawberries, white beans, sugar beets, roses, outdoor ornamental plants, aspen, poplar, and turf.

Comment: Nisso proposes to limit the maximum number of applications of thiophanate methyl to two applications per crop with the exception of mushrooms which can be limited to one application per crop and turf where the lower rates can be applied twice per season and a high rate can be applied only once per season.

PMRA's Response: The previous assessment (REV2007-12) was based on estimates for the use pattern. Since the number of applications was unknown, high end assumptions were made. Now that the product is limited to 2 applications per crop per season for most crops, all assessments were recalculated using the new maximum number of applications.

Comment: Nisso proposes that the personal protective equipment (PPE) for mixer/loader/applicators using Senator 70 WP WSB products include: long-sleeved shirt and long pants, chemical-resistant gloves made from any waterproof material and shoes plus socks. For those users of the loose wettable powder, PPE will remain as is currently labelled: chemical resistant coveralls over long sleeved shirt and long pants, chemical resistant gloves, rubber boots, goggles or face shield and NIOSH/MSHA approved N, R, P or HE respirator during mixing/loading/application.

PMRA's Response: PMRA will recommend appropriate PPE based on the risk assessment at the outcome of this re-evaluation process.

Comment: Nisso proposes to eliminate the use of the 17.5 kg a.i./ha rate (e.g. current maximum) for powdery mildew control on turf. The next highest rate on the label is 12.25 kg a.i./ha in single application per season for control of pink snow mould on turf.

PMRA's Response: The occupational mix/load/apply assessment has been updated based on the lowered rate of 12.25 kg a.i./ha on turf.

Comment: The highest rate on turf (12.25 kg a.i./ha) would have limited exposure since it is applied late in the year prior to snow cover and therefore has little chance for exposure to workers or golfers during the winter months. We request that this use pattern be used in subsequent risk assessments.

PMRA's Response: The postapplication assessment has been updated to reflect this use pattern. The lower rate used mostly on golf courses during the regular season (4.2 kg a.i./ha) has been used for the postapplication cancer assessment to workers and golfers.

Comment: DACO 5.4 or 5.5 Data Requirement. The AHETF will be generating exposure data for >30 mixer/loader/applicator scenarios. Nippon Soda Co., Ltd. is a member of the Agriculture Handlers Exposure Task Force and it is our understanding that PMRA acknowledges this task force.

PMRA's Response: The PMRA does acknowledge this task force and will make use of any relevant studies once they are reviewed and available for use.

Comment: DACO 5.8 Data Requirement. The EPA estimates a dermal absorption rate of 7% for Thiophanate methyl based on the results of an oral developmental toxicity study and a 21-day dermal toxicity study in the same species with similar endpoints.

PMRA's Response: The PMRA does not determine dermal absorption for TPM in this manner. In the absence of a chemical specific *in vivo* dermal absorption study, PMRA relies on a weight-of-evidence approach using all available data and information to estimate dermal absorption, which is considered more appropriate and scientifically valid.

Comment: DACO 5.8 Data Requirement. The USEPA estimated a dermal absorption rate of 3.5% for MBC (carbendazim) based on a dermal absorption study with benomyl. The EPA used benomyl as a surrogate compound because of similarities in toxicological effects and structure between benomyl and MBC.

PMRA's Response: The PMRA does not determine dermal absorption for carbendazim in this manner. In the absence of a chemical specific *in vivo* dermal absorption study, PMRA relies on a weight-of-evidence approach using all available data and information to estimate dermal absorption, which is considered more appropriate and scientifically valid.

Comment: DACO 5.8 Data Requirement. The registrant has an *in vitro* study with thiophanate methyl, using human skin, produced in Europe. A copy of the study was submitted to PMRA. The registrant would like the opportunity to discuss the results of this study, as there is no plan to conduct the specific study requested by the PMRA.

PMRA's Response: PMRA acknowledges receipt of the study and will review accordingly. As mentioned above, the study will be used as part of the weight-of-evidence approach to assess the dermal absorption of thiophanate-methyl.

Please note that PMRA reviews *in vitro* dermal absorption studies and considers them as supportive evidence in risk assessments. PMRA does not use the results of *in vitro* dermal absorption studies quantitatively to refine a value for dermal absorption in a risk assessment. Therefore, the submission of a rat *in vivo* study for dermal absorption is strongly recommended.

PMRA is in the process of considering *in vitro* data from rats and humans, as part of a triple pack which includes an *in vivo* rat study. The *in vitro* studies using rat and human skin may then be compared to the *in vivo* study. The *in vitro* studies need to be conducted under similar conditions as the *in vivo* study results and all three studies need to be conducted under conditions as would be seen in the field (eg., dose, formulation) to the extent possible.

The dermal absorption value for TPM (thiophanate-methyl) and CAZ (carbendazim) has already been refined from 100% to 25% using a weight-of-evidence approach in the absence of an *in vivo* study. It is unlikely that it will be refined further in the absence of an *in vivo* study.

Comment: The highest rate of TPM used on golf courses would be used during the fall for control of pink snow mold at 8.75 kg a.i./ha.

PMRA's Response: The updated risk assessment assesses mix/load/apply at the highest rate available for pink snow mould which is 12.25 kg a.i./ha. However, PMRA recognises that there will be little postapplication exposure to this high level as the golf season will be over, so all of the intermediate and long term post application scenarios have been revised and have been assessed using the lower rate for control of brown patch (4.2 kg a.i./ha).

Comment: Flower's Canada Grower's commented that concerns expressed around the occupational exposure of greenhouse ornamental workers can be resolved through application of refined transfer coefficient values and a thorough understanding of greenhouse production methodology.

PMRA's Response: Refined transfer coefficient values have been used in this assessment for all potted ornamentals and greenhouse cut flowers. PMRA welcomes the submission of any greenhouse production methodology, especially related to drench treatment of potted ornamentals.

Comment: 8 hours of mowing is used in the assessment. However, I would like to point out that there would not be 8 hours of exposure when mowing golf course tees and greens. Greens and tees are mowed by separate crews and takes 2 – 3 hours to mow greens and 2 hours to mow tees daily. It would take approximately 8 hours to mow fairways per day..... typically Senator 70 WP applications are not made to the fairways for this disease.

PMRA's Response: The post application risk assessment has been refined and now uses 3 hours of mowing time daily. To ensure that workers are not mowing for longer periods of time the following label statement has been added.

"Turf use is for golf course greens and tees only."

Comments Pertaining to Dietary/Drinking Water Exposure:

Comment: Regarding DACO 6.2 the registrant has conducted hen and goat metabolism studies, which can be submitted. The registrant asks the PMRA to clarify the specific metabolism data that are being sought.

PMRA Response: PMRA acknowledges receipt of these studies and will review them accordingly.

Comment: Regarding DACO 7.2 the registrant can obtain the analytical method and submit the method to the PMRA.

PMRA Response: PMRA acknowledges receipt of this data. However, the data do not comply with the Regulatory Directive DIR98-02 *Residue Chemistry Guidelines* (i.e. no values for recoveries, no inter-laboratory analytical methodology validation). Also, there is no method for animal tissues. Therefore, this data requirement for analytical methods for plant and animal tissues is still outstanding.

Comment: Regarding DACO 7.3 the registrant can obtain the freezer storage stability data from another company and submit the studies to the PMRA. Regarding carbendazim, a study is on-going for 5 years and will be done by 2011.

PMRA Response: PMRA acknowledges receipt of the freezer storage stability studies and will review them accordingly. The registrant should submit the 5 years storage stability study for carbendazim when available and confirm that the stability of thiophanate-methyl is similar under frozen and room temperature conditions.

Comment: Regarding DACO 7.4 a list of the contemporary field trial data for domestic and import uses was provided. These data must first be obtained by another company.

PMRA Response: A list with the residue trials conducted for the USEPA was sent to PMRA. PMRA will identify the required studies from this list. A formal request for these studies will be made by PMRA.

Comment: Regarding DACO 7.5 contemporary residue data for livestock and poultry can be supplied.

PMRA Response: PMRA acknowledges receipt of these studies and will review them accordingly.

Comment: The registrant wishes to know how they will be affected by the revocation of the 0.1 ppm as a general MRL for food pesticide residues.

PMRA Response: As noted in DIS2006-01, the intent is to specify replacement MRLs at or below 0.1 ppm for those registered pesticide/crop combinations for which residues have historically been covered under the 0.1 ppm general MRL.

Interested parties may also request Health Canada’s PMRA to amend or establish new MRLs, provided an application is made to do so and adequate data is submitted. MRLs are set only after Health Canada’s PMRA has confirmed that any pesticide residues that could be consumed are acceptable.

Comments Pertaining to Value: Comments on disease control on floral crops.
Senator 70WP is important for disease management programs used to control stem, root and crown rots caused by Rhizoctonia and Fusarium, as well as Botrytis, powdery mildews and leaf spot related diseases on floral crops. Senator 70WP is one of the most effective fungicides available with few alternatives equal to it that can be used in rotation to reduce resistance buildup by the target pests to various pest management products.

Response: Appendix III in REV2007-12 identifies the use of thiophanate-methyl on potted ornamental crops for the control of several soil-borne and foliar diseases as being an important use. As stated in Appendix III, the PMRA concurs that although there are some registered alternatives for all soil-borne and foliar diseases listed on the Senator 70WP label, no single active ingredient has a pest control spectrum equivalent to thiophanate methyl. Furthermore, in contrast to most alternative products, Senator 70WP can be applied on all species of potted ornamental plants which makes it a flexible tool that can be used in rotation with other registered fungicides to prevent or delay the development of fungicide resistance. The systemic nature of thiophanate-methyl allows translocation of the fungicide to the site of infection by two means of application: drench for soil-borne diseases and foliar spray for foliar diseases.

Comments on limited alternatives on floral crops

Fusarium and powdery mildew were recently identified by Canadian flower growers for the third year in a row as high priority diseases for which new effective controls must be found. Mycostop, a microbial fungicide, is available only for Fusarium control among the above diseases. Rhapsody, a recently registered microbial fungicide will suppress or control powdery mildew, Botrytis and some leaf spots only. There are, however, insufficient numbers of this new class of microbial fungicides in the registration system to help flower growers at this time.

Response: Fusarium wilt and powdery mildew were on the list of the grower-proposed priorities at the 2008 minor use priorities setting workshop and both were highly ranked by Ontario growers. For Fusarium stem, crown and root rots, the currently registered alternatives are listed under Appendix III in REV2007-12. The PMRA agrees that in general, microbial fungicides tend to have reduced potency and spectrum of control versus conventional fungicides. Currently, only a few microbial fungicides are registered for use on potted ornamentals, however, the PMRA and other stakeholders are making great efforts to facilitate faster registration of reduced risk pesticides such as these.

Need for thiophanate-methyl for control of Botrytis on flowers

Alternatives to Senator 70WP include dichloran, chlorothalonil, captan and quintozene, which are also under reevaluation with the PMRA. Two alternative products available for Botrytis control are labelled only for a handful of flower species severely limiting their usefulness. Loss of thiophanate-methyl in the greenhouse ornamental industry will reduce the number of effective products available for disease control.

Response: The alternative active ingredients dichloran, chlorothalonil, captan and quintozene cited in Appendix III of REV2007-12 are currently under re-evaluation. Three alternative active ingredients available for control of Botrytis on greenhouse ornamentals are listed in Appendix III of REV2007-12. While dichloran and chlorothalonil are registered only for use on a limited number of important flowering greenhouse ornamental species where Botrytis is a common problem, the fenhexamid label allows the use of this active ingredient on “all species and cultivars”.

Need for the same products for floriculture as registered in the USA
The USA is a major growing marketplace for Canadian potted plants and flowers. Our USA counterparts have Cleary's 3336, that contains the same active ingredient as Senator 70WP, for use in greenhouses as well as other fungicides not currently registered in Canada. It is critical that ornamental growers in Canada have the same tools available as those in the USA to adequately control these important diseases and to ensure that Canadians become competitive in the international marketplace. We request that the PMRA consider the value of Senator 70WP for our industry during the re-evaluation of thiophanate-methyl.

Response: The PMRA has acknowledged and is currently addressing the technology gap between the USA and Canada. The smaller size of the Canadian horticultural pesticide market which drives the number of applications for registration and approved products remains a challenge. Efforts to minimize the effect of this technology gap on competitiveness of Canadian growers are being pursued. The PMRA and other stakeholders are implementing several programs and policies to facilitate faster registration of products requested by users, including reduced risk products. Since the publication of REV2007-12, the PMRA has received many comments and new information from various stakeholders. The registrant has proposed some changes to the use pattern, that the PMRA has considered, as well as some new information with which to refine its risk and value assessments. As appropriate, the PMRA will continue its dialogue with stakeholders about potential mitigation and transition strategies to avoid or minimize potential detrimental impacts on the industry.

Letter of support and comments concerning the importance of thiophanate-methyl for the dry bean production and the seed production and treatment industry
Thiophanate-methyl is the most effective systemic product registered for use on dry common beans for the control of seed borne anthracnose, a devastating disease for dry bean growers. Alternatives to DCT Dual Purpose Seed Treatment Powder include carbathiin, thiram and fludioxonil+metalaxyl-M, which are also under re-evaluation with the PMRA. Loss of DCT in the dry bean seed industry would reduce the number of effective products available for the control of seed borne anthracnose. At this time when resistance to new classes of fungicides needs to be managed, it is important to have access to effective chemistries such as thiophanate-methyl. We urge the PMRA to carefully undertake the re-evaluation of thiophanate-methyl and consider its importance to our industry.

Response: The PMRA agrees that the systemic translocation of thiophanate-methyl, especially in rapidly developing tissue such as germinating seeds, makes it a very important tool for the dry bean industry to manage seed-borne anthracnose. Thiophanate-methyl is especially of value to Canadian seed producers in the production of high quality clean seeds. While some of the alternative active ingredients cited in Appendix III of REV2007-12 are still under re-evaluation, the re-evaluation of metalaxyl-M is complete and this active ingredient has been granted continued registration as announced in RVD2008-03. Fludioxonil which is co-formulated with metalaxyl-M was first registered in 2002 and is not currently under re-evaluation. The PMRA agrees that although the seed treatment use of thiophanate-methyl on dry beans has a low agronomic risk factor for the development of fungicide resistance based on the FRAC (Fungicide Resistance Action Committee) classification scheme, thiophanate-methyl contributes to pest management and sustainability by allowing rotation and dual application with new classes of fungicides.

Letter of support and comments concerning the importance of thiophanate-methyl for the potato production and seed potato industry

Senator PSPT, its drying capabilities, its disease control spectrum and its mode of action are very important tools for the potato industry during the planting season. There are only two active ingredients, being thiophanate-methyl and fludioxonil, in potato seed piece treatment formulations registered in Canada that provide systemic control of potato seed borne diseases and are labeled for control of the disease silver scurf. Senator PSPT (containing thiophanate-methyl) is the only potato seed piece treatment registered for control of the disease verticillium wilt. At this time when resistance to new classes of fungicides needs to be managed, it is important to have access to effective chemistries such as thiophanate-methyl. In addition, only Senator PSPT and Maxim PSP (containing fludioxonil) provide growers with the opportunity to treat potato seed pieces early in the season, prior to planting, permitting them to be stored until required.

Response: The PMRA agrees that although there are registered alternatives to thiophanate-methyl potato cut-seed treatment, the systemic mode of action and wide control spectrum of thiophanate-methyl contributes to pest management and sustainability by allowing growers to rotate potato seed treatment fungicides among the few available alternatives. Fungicide resistance management is becoming increasingly important for the potato industry as there is growing concern for fungicide resistance development in several seed-borne pathogens. Other benefits of the dust or powder formulation may also include use and storage well ahead of planting and a contribution to the process of potato seed-piece curing. As listed in Appendix XI, fludioxonil is the only alternative active ingredient registered for the control of silver scurf, a major disease of potato that has become more prevalent during the last decade. Reports of strains of *Helminthosporium solani* that are resistant to both thiophanate-methyl and fluodioxonil have recently raised some concerns for the need to develop and adopt improved resistance management practices. The PMRA is proposing to strengthen the voluntary resistance management statements on the Senator PSPT and other potato seed piece treatment product labels containing thiophanate-methyl. The active ingredients captan and thiophanate-methyl are both registered potato seed piece treatments for the control of verticillium wilt, however, the former provides suppression only.

Comments concerning the continued effectiveness of thiophanate-methyl on two potato diseases: Fusarium dry rot and silver scurf

Effective fungicide seed piece treatments are an important tool for controlling diseases like Fusarium dry rot, silver scurf, and Rhizoctonia stem and stolon canker. There are few products available for control of these diseases, and product choice is further limited due to the development of fungicide resistant pathogens. For these reasons, it is important that Canadian potato producers have access to effective fungicide seed piece treatments as one tool to manage seed borne diseases. Availability of seed piece treatments from different chemical groups is also important to reduce and delay the development of fungicide resistance.

Thiophanate-methyl is registered for control of both Fusarium dry rot and silver scurf. In recent years, questions have arisen regarding the efficacy of this product against these two pathogens, given the widespread resistance toward thiabendazole, a related chemistry. It is necessary to have current information regarding the efficacy of thiophanate-methyl on the labeled diseases.

Response: Canadian researchers have reported resistance to thiabendazole and thiophanate-methyl in some Canadian isolates of *Fusarium sambucinum* and *Helminthosporium solani*, which cause fusarium dry rot and silver scurf respectively in potato (Peters, *et al.*, 2008). They have recommended consideration and adoption of resistance management strategies and further resistance testing in Canadian potato production areas. The PMRA is recommending the upgrading of the voluntary resistance management statements on the Senator PSPT and other potato seed piece treatment product labels containing thiophanate-methyl.

Comments received concerning the maximum label rate of 17.5 kg a.i./ha for powdery mildew control, a disease of turf species not commonly requiring control on Canadian turf
The rate used in the preliminary risk assessment is the highest rate listed on the Senator WSB label, being 17.5 kg a.i./ha for the control of powdery mildew. This may be misleading and it should be noted that the highest rate of thiophanate-methyl used on golf courses would be used during the fall for control of pink snow mold at 8.75 kg a.i./ha. Although there are alternative fungicides available to the turf industry, thiophanate-methyl is important as a rotation chemistry for resistance management purposes. In our experience, Senator WSB is typically applied twice per year in the rotation of fungicides. It may be applied three times during a high disease pressure season. We request that the PMRA better reflect the turf industry use of thiophanate-methyl in the risk assessment. We also request that the PMRA give consideration to the value of Senator WSB within the turf industry.

Response : The PMRA acknowledges the turf industry's support for thiophanate-methyl and the rates typically used on Canadian golf courses. In REV2007-12, the PMRA has used the maximum label rate for turf that was supported at that time. Since its publication, the registrant has informed the PMRA that it no longer supports the use of thiophanate-methyl for powdery mildew control on turf, thus effectively limiting the maximum single application rate on turf to 12.25 kg a.i./ha, instead of the maximum label rate for powdery mildew control of 17.5 kg a.i./ha. All other uses on turf are supported by the registrant with some mitigation measures including packaging of the end use products targeted to the turf sector in water soluble bags, reducing the maximum label application rate on turf, and limiting the maximum number of applications to three per season, only one of which could be at the maximum supported application rate of 12.25 kg a.i./ha. The current refined risk and value assessments have taken into account the use profile currently supported by the registrant.

Comments Pertaining to the Environmental Assessment:

Comment From Nisso: The registrant is submitting earthworm acute toxicology data and 2 field studies. These data were submitted to the EU as part of the submission to place thiophanate-methyl on Annex 1 as per EU 91/414.

Response: These studies, which were reviewed by PMRA, consisted of two laboratory studies and two field studies. The two field studies did not provide adequate information for a risk assessment.

One of the laboratory studies that had a duration of eight weeks, was on growth and reproduction of the earthworm *Eisenia fetidia* [PMRA # 1530416, Report No RD-00146 Effects of Thiophanate-methyl on reproduction and growth of *Eisenia fetidia* (Savigny 1826) in artificial soil (Ralf Pettro, 1998)]. At TPM application rates of up to 0.6 kg a.i./ha there were no reductions in body weight but at 0.8 and 1.2 kg a.i./ha there were reductions. Reductions in body weight from carbendazim occurred at 0.15 kg a.i./ha. At 1.2 kg a.i./ha body weight gain stopped altogether. At TPM application rates of up to 0.6 kg a.i./ha there was no effect on reproduction but reductions in reproduction occurred at 0.8 and 1.2 kg a.i./ha. Reductions in reproduction from carbendazim occurred at 0.15 kg a.i./ha and these increased to 71% at 1.2 kg a.i./ha. Therefore, for carbendazim the chronic LOEC is approximately 0.15 kg a.i./ha. A NOEC was not clearly established. For thiophanate-methyl the chronic NOEC is 0.60 kg a.i./ha. The risk assessment (shown below) indicates that the Level of Concern for chronic effects from thiophanate methyl is exceeded at all but the lowest application rate. For carbendazim the level of concern is exceeded at all application rates. Therefore, chronic effects on earthworm growth and reproduction are likely to occur with the use of thiophanate-methyl and its transformation product MBC (the abbreviation used for carbendazim by USEPA).

Earthworm Chronic Effects Risk Assessment for Thiophanate-methyl and Carbendazim (PMRA # 1530416)

TPM Appl. Rate × No Appl. kg a.i./ha	Cumulative Appl. Rate TPM kg a.i./ha	TPM RQ= Cum. Appl. Rate/NOEC	LOC (RQ =1)	Equivalent Cum. Appl. Rate MBC kg a.i./ha	MBC RQ= Cum. Appl. Rate/NOEC	LOC (RQ =1)
0.392 × 2	0.395	0.7	Not exceeded	0.359	2.4	Exceeded
0.77 × 2	0.776	1.3	Exceeded	0.705	4.7	Exceeded
0.77 × 3	0.776	1.3	Exceeded	1.049	7	Exceeded
1.225 × 2	1.378	2.3	Exceeded	1.121	7.5	Exceeded
1.575 × 2	1.587	2.6	Exceeded	1.443	9.6	Exceeded
17.5 × 1	17.5	29.2	Exceeded	8.076	53.8	Exceeded
Half life TPM soil = 1 d. Half life MBC soil = 320 d. TPM NOEC = 0.60 kg a.i./ha. MBC LOEC = 0.15 kg a.i./ha.						

* MBC: the abbreviation used for carbendazim by USEPA

The second laboratory study (PMRA # 1530417) tested the effects of thiophanate-methyl on the earthworm *Eisenia foetida* over a time period of 14 days. At a maximum concentration in soil of 162 mg a.i./kg, there was no mortality of the test earthworms. However, there were reductions in body weight of the earthworms from 18 mg a.i./kg. NOEC was 18 mg a.i./kg and NOEC was 6 mg a.i./kg. The risk assessment indicated below showed that there was negligible acute risk to earthworms based on mortality. The chronic risk based on reduction in body weight also showed that the risk was negligible, including at the reduced proposed rate of 12.25 kg a.i./ha.

Earthworm Acute and Chronic Risk Assessment for Thiophanate-methyl (PMRA # 1530417)

TPM Appl. Rate × No Appl. kg a.i./ha	Cum Appl. Rate TPM kg a.i./ha	EEC mg a.i./kg soil	TPM RQ= EEC/ $0.5×EC_{50}$	LOC (RQ =1) Exceeded	TPM RQ= EEC/NOEC	LOC (RQ =1) Exceeded
0.392 × 2	0.395	0.176	0.002	No	0.029	No
0.77 × 2	0.776	0.345	0.004	No	0.058	No
0.77 × 3	0.776	0.345	0.004	No	0.058	No
1.225 × 2	1.378	0.612	0.008	No	0.102	No
1.575 × 2	1.587	0.705	0.009	No	0.118	No
17.5 × 1	17.5	7.776	0.096	No	**1.3**	Yes
12.25 × 1	12.25	5.444	0.067	No	0.91	No
Half life TPM soil = 1 d. Half life MBC soil = 320 d. TPM 0.5 ×EC50 = 81 mg a.i./kg soil. TPM NOEC = 6 mg a.i./kg soil. (PMRA 1530417)						

* MBC: the abbreviation used for carbendazim by USEPA

Comment From Nisso: A 28-day chronic toxicity study on the rainbow trout was conducted and is included with this submission. The study resulted in a NOEC of 0.32 ppm.

Response: The study (PMRA # 1530423) was reviewed and deemed to be acceptable. Using the endpoint from the early life cycle study for rainbow trout for thiophanate-methyl provided by Nisso (0.32 mg a.i./L), the screening level risk assessment indicated a risk (RQ 4.8) at the maximum proposed application rate of 12.25 kg a.i./ha. However, a refined risk assessment based on exposure to spray drift (11% of applied rate) showed negligible risk (RQ 0.53). In addition, a refined risk based on exposure from runoff also showed negligible risk (RQ 0.25).

Risk to Rainbow trout based on Early Life Cycle toxicity from Thiophanate-methyl

Risk Assessment	Appl. Rate TPM kg a.i./ha	EEC, mg a.i./L	Early life stage NOEC mg a.i./L	ELC RQ = EEC/NOEC	LOC (RQ = 1)
Screening level	12.25 × 1	1.53	0.32	**4.8**	**Exceeded**
Refined level: Spray drift	12.25 × 1	0.169	0.32	0.53	Not exceeded
Refined level: Runoff	12.25 × 1	80.5×10^{-3}	0.32	0.25	Not Exceeded

Comment from Nisso: EPA mentioned a chronic (early life stage) sheepshead minnow study in the RED; however, the study was not officially requested. During a meeting among PMRA, Nisso and Engage Agro on June 20, 2007 it was determined that PMRA no longer requests this study. Therefore, there are no plans to conduct this study.

Response: Based on the results of the risk assessment for freshwater fish, it is unlikely that thiophanate-methyl will be a risk to estuarine marine fish.

Comment from Nisso: Nisso raises questions about the Koc value that was used by the PMRA in its model estimations of groundwater and surface water concentrations of carbendazim (transformation product of thiophanate-methyl). Nisso pointed out that the USEPA chose a Koc value of either 2100 (RED value) or 1885 (EPA/EFED “science chapter” value) in its water modelling, while the PMRA used a Koc value of 305.

Response: In conducting its re-evaluation, the PMRA relied upon information in the USEPA RED. The RED contains references to three adsorption/desorption studies:

- MRID 42351001, (Shiotani, H. 1992) Leaching/Adsorption/Desorption (Nisso)
- ACC. 00151421, (DuPont), Leaching/Adsorption/Desorption
- ACC. 00151422, (DuPont), Leaching/Adsorption/Desorption

However, the RED Science Chapter’s Appendix 5 (Environmental Fate Reviews for TPM) only provided a Data Evaluation Record (DER) of the first study, MRID 42351001. The PMRA calculated Koc values for the six soils in this study, which were similar to EPA’s values for this study. The PMRA used the smallest value of the six (Koc =305) in its 2005 water modelling, consistent with the approach for Level 1 at the time. Conversely, the EPA did not use the Koc values for carbendazim from MRID 42351001 in its water modelling, but rather used a Koc value from one or both of the other two studies. These studies were conducted by DuPont and used benomyl, which transforms to carbendazim. It was not clear from the USEPA RED why the results from the first study (MRID 42351001) were not also considered, as the DER concluded the study was acceptable.

Upon receipt of Nisso’s comments, the PMRA requested the three studies referenced above, to review adsorption/desorption values. Nisso was only able to provide the first study, as the latter two were conducted by DuPont. The PMRA has re-analyzed the first study and obtained similar Koc values for carbendazim to those used in previous modelling. Based on current approaches for choosing a Koc for modelling, the Koc value for carbendazim is 429, which is not very different from that used in the previous PMRA modelling (305), and is furthermore somewhat larger than most of the values cited by the European Union (EU) as indicated in Table 1.

Table 1 Comparison of Koc values used by the USEPA, the EU, and the PMRA.

Source of Data	Koc values	
	Thiophanate-Methyl (TPM)	Carbendazim (or MBC*)
USEPA [1]	314	1885
EU	189 - 225 [2] 189 - 225 [3]	200 - 246 [2] 375 - 1090 [3]
PMRA Level 1	71.2	305
PMRA Level 2	100	355
PMRA Recalculated [4]	91	429

* MBC: the abbreviation used for carbendazim by USEPA

(1) USEPA, May 9, 2001, Revised EFED RED document for thiophanate-methyl and its major degradate,

(2) EU Footprint Pesticides Properties Database. Accessed at: http://sitem.herts.ac.uk/aeru/footprint/en/index.htm

(3) EU Review report for the active substance thiophanate-methyl, 5030/VI/98 final, 15 Feb 2005

(4) Recalculated Sept. 2008 from original study data (MRID 42351001, Shiotani, H. 1992). Value is the 20th percentile Koc from six soils.

As the USEPA Koc of 1885 comes from studies that Nisso is unable to produce, the PMRA cannot consider this value in its modelling. However, even if the benomyl adsorption studies are produced, the PMRA's current approach for modelling is to use the 20th percentile Koc from all acceptable values; thus, adding one or two larger values (1885 and/or 2100) to the existing six values would not significantly change the 20th percentile.

Comment: Nisso is proposing to lower the maximum application rate from 17.5 kg a.i./ha to 12.25 kg a.i./ha.

Response: Lowering the maximum application rate from 17.5 kg a.i./ha to 12.25 kg a.i./ha should lower the risk quotients. Assessment o f risk at the new proposed maximum rate will be conducted.

Comment: Nisso provided a *Daphnia Magna* chronic toxicity study which showed a NOEC of 17.7 µg/L rather than 3 µg/L as reported in the RED.

Response: If the data provided in the study (PMRA # 1530460) is used, then the chronic risk quotient for *Daphnia magna* from carbendazim will drop from RQ = 34 to 5 at an application rate of 17.5 kg a.i./ha. If the application rate is further reduced from 17.5 to 12.25 kg a.i./ha then the risk quotient would be further reduced to about 3 which is slightly above the level of concern.

The value reported in the USEPA RED (3 µg/L) was from a core study provided to the USEPA and was considered by that agency to be acceptable. The policy of PMRA is to use the most conservative data available from an acceptable study.

Appendix II Additional Data Requirements

1. The following data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants of this active ingredient are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that will be sent to registrants of the technical active ingredients by the PMRA.

- Developmental neurotoxicity in rats (DACO 4.5.14)
- Developmental neurotoxicity in rats (DACO 4.5.14) for Carbendazim
- Mixer/loader/applicator - passive dosimetry data or biological monitoring data for on-farm potato seed treatment and planting (DACO 5.4/5.5)
- Mixer/loader/applicator - passive dosimetry data or biological monitoring data for dry common beans and sweet corn on-farm planting. Data from the Agricultural Handler Exposure Task Force (AHETF) may fill this data gap. This data is pending review (DACO 5.4/5.5)
- Mixer/loader/applicator - passive dosimetry data or biological monitoring data for commercial seed treatment (dry common beans and sweet corn).(DACO 5.4/5.5). AHETF data may fill this data gap.
- Enforcement Analytical Methodology for plant and animal matrices (not required if a valid multi-residue analytical methodology is submitted) (DACO 7.2.2)
- Inter-laboratory Analytical Methodology Validation (DACO 7.2.3)
- Multi-residue Analytical Methodology Evaluation (DACO 7.2.4)

2. The following data will be required for future uses:

DACO 7.4.1	Supervised Residue trial data for domestic and import uses
DACO 7.4.3	Confined Crop Rotation Data
DACO 7.4.4	Field Crop Rotation Trial Data
DACO 7.4.5	Processed Food/Feed data

Field Trial Data required from the registrants:
The registrant provided PMRA with an index of field trial data and processed food data that have been submitted to USEPA. The following studies are required in support of the Canadian registered food uses and MRLs:

Table 1 List of the Required Supervised Residue Trial data for domestic and import uses

Product	DACO No.	Author	Date (year)	Title
Senator 70WP	7.4.1	Leppert, I	1996	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Dry Bean
Senator 70WP	7.4.1	Carr, B.	1997	Thiophanate Methyl and Metabolites: Magnitude of Residue in Summer Squash
Senator 70WP	7.4.1	Bennett	1998	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Watermelon
Senator 70WP	7.4.1	Bradway	1999	Thiophanate Methyl and MBC: Magnitude of the Residue in Potato
Senator 70WP	7.4.1			Thiophanate Methyl: EPA Review of Residue Data in Beans, Cherry, Garlic, Onion, Peach and Wheat
Senator 70WP	7.4.1	Castro, L	1998	Thiophanate Methyl and Metabolites: Magnitude of Residue in Soybean
Senator 70WP	7.4.1	Bennett,	1998	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Cucumber
Senator 70WP	7.4.1	Carr, B.	1998	Thiophanate Methyl and Metabolites: Magnitude of the Residue in Pecans
Senator 70WP	7.4.1	Bradway	1998	Thiophanate Methyl and Metabolites: Magnitude of the Residue in Peanut
Senator 70WP	7.4.1	Artz, S.	1997	Magnitude of the Residue of Thiophanate-methyl and MBC in Blueberries Raw Agricultural Commodities Following Applications of TOPSIN M 70W
Senator 70WP	7.4.1	Malik, N.; Wright, M.	1992	Carbon 141-Thiophanate-Methyl Nature of the Residue in Spray Treated Lima Beans
Senator 70WP	7.4.1	Wright, M.	1996	(Carbon 14)-Thiophanate-Methyl Nature of the Residue in Spray Treated Lima Beans: Supplement No. 1 to Final Report.
Senator 70WP	7.4.1	Leppert	1996	Thiophanate Methyl and Metabolites: Magnitude of the Residue in Dry Bean
Senator 70WP	7.4.1	AlanAlam, F., Dedmore, M.; Jalal, M.	1994	Nature of the Residues of (carbon 14)-Thiophanate-Methyl in Spray Treated Apples
Senator 70WP	7.4.1	Malik, N.	1992	(Carbon 14)-Thiophanate-Methyl Nature of the Residue in Spray Treated Sugar Beets
Senator 70WP	7.4.1	Wright, M.	1996	Nature of the Residues of (carbon 14_-Thiophanate-Methyl in Spray Treated Sugar Beets: Supplement 1 to Final Report

Senator 70WP	7.4.1	Leppert,	1996	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Peach and Nectarine
Senator 70WP	7.4.1	Leppert,	1996	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Cherry
Senator 70WP	7.4.1	Leppert,	1996	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Snap Bean
				Crop Field Trials (Plums)
				Crop Field Trials (Prunes)
				Crop Field Trials (Mushrooms)
				Crop Field Trials (Pears)
				Crop Field Trials (Almonds)
				Crop Field Trials (Apricots)
				Crop Field Trials (Banana)
				Crop Field Trials (Citrus fruit)
				Crop Field Trials (Pistachios)
				Crop Field Trials (Pumpkins)
				Crop Field Trials (Strawberries)
				Crop Field Trials (Canola)
				Crop Field Trials (Grapes)
				Crop Field Trials (Peanuts)
				Crop Field Trials (Pineapple)
				Crop Field Trials (Raspberries)
				Crop Field Trials (Tomatoes)

* MBC: the abbreviation used for carbendazim by USEPA

Processed Food/Feed studies required from the registrants:
The registrant provided PMRA with an index of processed food data that has been submitted to USEPA. The following processed food/feed studies related to the Canadian registered domestic and imported crops are required:

Table 2 List of the Required Processed Food/Feed for domestic and import uses

Product	DACO No.	Author	Date (year)	Title
Senator 70WP	7.4.1	Castro, L	1998	Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Soybean Processed Commodities
Senator 70WP	7.4.5			Thiophanate Methyl and its Metabolites: Magnitude of the Residue in Potato Processed Commodities
Senator 70WP	7.4.5	Carr, B.	1998	Thiophanate Methyl and its Metabolites: Magnitude of the Residue Sugar Beet Processed Fractions
Senator 70WP	7.4.5	Carr, B.	1999	Thiophanate Methyl and its Metabolites: Magnitude of the Residue Peanut Processed Fractions
				Processed Food (Canola)
				Processed Food (Grape)
				Processed Food (Prunes)

Appendix III Registered thiophanate-methyl products as of October 22, 2008 [1]

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
12279	Commercial	Nippon Soda Company Ltd.	Senator 70 WP 1 Fungicide	WP-Wettable Powder	Thiophanate-methyl 70%
14599	Commercial	Nippon Soda Company Ltd.	Senator PSPT 1 Potato Seed Piece Treatment	DU-Dust or Powder	Thiophanate-methy1 10%
14986	Commercial	Norac Concepts Inc.	DCT Dual Purpose Seed Treatment Powder	WP-Wettable Powder	Thiophanate-methyl 14% Diazinon 6% Captan 18%
16660	Commercial	Agrium Advanced Technologies Rp Inc.	Proturf Granular Systemic Fungicide	GR-Granular	Thiophanate-methyl 2.3%
25343	Commercial	Nippon Soda Company Ltd.	Senator 70WP Systemic Fungicide	WP-Wettable Powder	Thiophanate-methyl 70%
26236	Commercial	Nippon Soda Company Ltd.	Senator PSPT Potato Seed Piece Treatment	DU-Dust or Powder	Thiophanate-methyl 10%
26987	Commercial	Norac Concepts Inc.	Caption CT Fungicide Seed Treatment Wettable Powder	WP-Wettable Powder	Thiophanate-methyl 14% Captan-18%
27297	Commercial	Nippon Soda Company Ltd.	Senator 70 WP WSB1 Fungicide	WP-Wettable Powder	Thiophanate-methyl 70%
28160	Commercial	Bayer Crop Science Inc.	Genesis XT Potato Seed-Piece Treatment	DU-Dust or Powder	Thiophanate-methyl 3% Imidacloprid 1.25% Mancozeb 6%
14851	Domestic	King Home and Garden Inc.	Gardal Rose, Flower, and Evergreen Dust	DU-Dust or Powder	Thiophanate-methyl 3% Malathion 4% Captan 5% Carbaryl 5%
27539	Manufacturing concentrate	Nippon Soda Company Ltd.	Senator 70WP MUP Systemic Fungicide	WP-Wettable Powder	Thiophanate-methyl 70%
22710	Technical	Nippon Soda Company Ltd.	Thiophanate-Methyl Technical	WP-Wettable Powder	Thiophanate-methyl 98.3%

[1] excluding discontinued products or products with a submission for discontinuation.

Appendix IVa Registered Commercial Class uses of thiophanate-methyl in Canada as of April 7, 2006 and rate and use pattern modifications proposed by the registrant in response to REV2007-12, updated October 22, 2008

Site(s)	Pests(s)	Marketing Class[1]	Formulation Type[2]	Application Methods and Equipment	Application Rate (g a.i./ha) unless otherwise stated		Proposed /Maximum Number of Applications per Year[3]	Proposed / Minimum Number of Days Between Applications [3]	Supported Use? [4]	Comments
					Maximum Single	Maximum Cumulative				
WP and DU products uses described in REV2007-12 are no longer supported by the registrant on most use site categories except USC 10- seed treatments food and feed. All uses of products are still supported by the registrant in water soluble bags (WSB), including those that were registered through an URMULE or an emergency use registration (not addressed in this re-evaluation document).										
USC 6 - greenhouse non-food (WSB packaging supported)										
Greenhouse potted ornamentals (drench)	Stem, crown and root rots caused by *Fusarium* and *Rhizoctonia*	C	WSB	Watering equipment	5 950	11 900	2	15	Y	Drench treatment assuming 10 000 L/ha of dilute solution applied per application.
Greenhouse potted ornamentals (foliar)	Powdery mildew, Botrytis and leaf spots	C	WSB	Ground, hydraulic sprayers	595	1 190	2	7	Y	Foliar application with hydraulic spraying equipment.
USC 10 - seed treatments food and feed (DU and WP formulation supported)										
Potatoes (seed treatment-cut seed)	Verticillium wilt, fusarium rot, silver scurf (*Helmintho-sporium solani*), and aids in control of seed piece decay and black leg infections	C	DU	Dry seed treatment container or seeder box	1 160 (assuming seeding rate of 2320 kg/ha of cut-seed)	1 160 (assuming seeding rate of 2320 kg/ha of cut-seed)	1	not applicable	Y, M (silver scurf only)	The use for the control of silver scurf was registered through an URMULE
Dry common bean (seed treatment)	Seedborne anthrachnose	C	WP	Slurry machines or hand mixing with paddle or shovel	42	42	1	not applicable	Y	

Site(s)	Pests(s)	Marketing Class[1]	Formulation Type[2]	Application Methods and Equipment	Application Rate (g a.i./ha) unless otherwise stated		Proposed /Maximum Number of Applications per Year[3]	Proposed / Minimum Number of Days Between Applications [3]	Supported Use? [4]	Comments
					Maximum Single	Maximum Cumulative				
Sweet corn (seed treatment)	Seedborne *Penicillium* spp.	C	WP	Seed box treatment	not available (14.7 g assuming seeding rate of 21 kg/ha)	not available (14.7 g assuming seeding rate of 21 kg/ha)	1	not applicable	Y	
USC 14- terrestrial food crops (WSB packaging supported)										
Apples and pears (Eastern Canada and BC)	Apple scab, powdery mildew	C	WSB	Ground, hydraulic sprayers	1 575 (BC only) or 437.5 (Eastern provinces)	3 150 (BC only) or 875 (Eastern provinces)	[2]	[7]	Y	Typically no more than 2 applications are made per year. A third application is rare. In response to REV 2007-12, the registrant has proposed to reduce the maximum number of applications to 2 and increase the minimum interval between applications to 7 days. Minimum interval between applications is 5 days from the label.
Lowbush blueberries	Blossom and twig blight	C	WSB	Ground and Aerial hydraulic sprayers	770	1 540	[2]	10	Y, M	Typically no more than 2 applications are made per year. In response to REV 2007-12, the registrant has proposed to reduce the maximum number of applications to 2 per year.
Peaches, nectarines, plums, prunes, cherries	Brown rot	C	WSB	Ground, hydraulic sprayers	1 225	2 450	[2]	[7]	Y	Typically no more than 2 applications are made per year. In response to REV 2007-12, the registrant has proposed to reduce the maximum number of applications to 2 per year, and increase the minimum interval between applications to 7 days.

Site(s)	Pests(s)	Marketing Class[1]	Formulation Type[2]	Application Methods and Equipment	Application Rate (g a.i./ha) unless otherwise stated		Proposed /Maximum Number of Applications per Year[3]	Proposed / Minimum Number of Days Between Applications [3]	Supported Use? [4]	Comments
					Maximum Single	Maximum Cumulative				
Raspberries	Powdery mildew, fruit rots	C	WSB	Ground, hydraulic sprayers	770	1 540	[2]	7	Y	Typically no more than 2 applications are necessary per year. In response to REV2007-12, the registrant has proposed to reduce the maximum number of applications to 2 per year.
Strawberries	Fruit rot (*Botrytis* sp.), Leaf spot	C	WSB	Ground, hydraulic sprayers	770	1 540	[2]	[7]	Y	Typically no more than 2 applications are necessary per year. In response to REV 2007-12, the registrant has proposed to reduce the maximum number of applications to 2 per year, and increase the minimum interval between applications to 7 days.
White beans	White mould	C	WSB	Ground and Aerial sprayers	1 575	3 150	2	[7]	Y	
Sugar beets (for export only)	Leaf spot (*Cercospora* sp.)	C	WSB	Ground, hydraulic sprayers	392	784	2	[7]	Y, M	Only applied to sugar beets for export
USC 27 - ornamentals outdoor (WSB packaging supported)										
Roses, ornamental plants	Black spot, powdery mildew, and certain other diseases	C	WSB	Ground, hydraulic sprayers	525	1 050	[2]	10	Y	In response to REV 2007-12, the registrant has proposed to reduce the maximum number of applications to 2 per year.

Site(s)	Pests(s)	Marketing Class[1]	Formulation Type[2]	Application Methods and Equipment	Application Rate (g a.i./ha) unless otherwise stated		Proposed /Maximum Number of Applications per Year[3]	Proposed / Minimum Number of Days Between Applications [3]	Supported Use? [4]	Comments
					Maximum Single	Maximum Cumulative				
Aspen and poplar	Marssonnina and septoria leaf spots	C	WSB	Ground, hydraulic sprayers	770	1 540	[2]	10	Y	In response to REV 2007-12, the registrant has proposed to reduce the maximum number of applications to 2 per year.
USC 30 - Turf (WSB packaging supported, no packaging change for GR products)										
Turf	Brown patch (*Rhizoctonia solani*)	C	WSB	Ground, hydraulic sprayers	4.2 kg a.i./ha	8.4 kg a.i./ha	[2]	[7]	Y	In response to REV 2007-12, the registrant has proposed that the maximum number of applications for this pest be 2 per year. The maximum number of applications for all pests on this site should not exceed 3 per year (only one of which can be at the high rate for control of pink snow mould), and that the minimum interval between applications be increased to 7 days.
Turf	Pink snow mould (*Fusarium nivale*)	C	WSB	Ground, hydraulic sprayers	12.25 kg a.i./ha	12.25 kg a.i./ha	[1]	Not Applicable	Y	In response to REV 2007-12, the registrant has proposed that the maximum number of applications for this pest be 1 per year. The maximum number of applications for all pests on this site should not exceed 3 per year.

Site(s)	Pests(s)	Marketing Class[1]	Formulation Type[2]	Application Methods and Equipment	Application Rate (g a.i./ha) unless otherwise stated		Proposed /Maximum Number of Applications per Year[3]	Proposed / Minimum Number of Days Between Applications [3]	Supported Use? [4]	Comments
					Maximum Single	Maximum Cumulative				
Turfgrass	Brownpatch, dollar spot and copper spot	C	GR	Ground spreader	3.04 kg a.i./ha	[6.08] kg a.i./ha	[2 to 4 depending of rate(s) used]	14	Y	In response to REV 2007-12, the registrant has proposed that the "*Maximum application* (cumulative rate) *per season must not exceed 6.08 kg a.i./ha*). A granular fertilizer-fungicide product containing thiophanate-methyl is registered in Canada under the *Fertilizers Act.*

1 C = Commercial, D = Domestic
2 WP=Wettable Powder, DU=Dust or Powder, GR=Granular, WSB = Water Soluble Bags
3 Values in brackets [ ] indicate number proposed by the technical registrant
4 Y = use is supported by the registrant, M = use was registered as a User Requested Minor Use Label Expansion (URMULE).

Appendix IVb Registered Domestic Class uses of thiophanate-methyl in Canada as of as of April 7, 2006 and proposed rate and use pattern modifications in response to REV2007-12

Site(s)	Pests(s)	Formulation Type[1]	Application Methods and Equipment	Application Rate (g a.i./ha)		Maximum Number of Applications per Year [2]	Typical Number of Days Between Applications [2]	Supported Use? [3]	Comments
				Maximum Single	Maximum Cumulative				
The use of DU Domestic products is supported by the registrant. There is no change to the use pattern.									
USC 27 - ornamentals outdoor									
Roses, flowers and ornamentals (domestic class)	black spot, powdery mildew	DU	Ground, squeeze duster	Not Listed	Not Listed	Not Listed [Typically 6]	[Typically 10]	Y	
Junipers (domestic class)	blight	DU	Ground, squeeze duster	Not Listed	Not Listed	Not Listed [Typically 6]	[Typically 10]	Y	

[1] DU=Dust or Powder,
[2] Values in brackets [ ] indicate number proposed by the end-use product registrant
[3] Y = use is supported by the registrant.

Appendix V

Table 1 Toxicology endpoints for thiophanate-methyl health risk assessment

Exposure Scenario	Dose (mg/kg bw/day)	Endpoint	Study	UF or MOE
Acute Dietary General Population	NOAEL = 40	Tremors 2-4 hrs post-dosing	1 year - Dog	300 (3x for lack of acute neurotox)
	ARD =0.13 mg/kg bw			
Acute Dietary Females 13-50	NOAEL = 20	Multiple supernumary ribs	Developmental Toxicity - Rabbit	300 (3x for lack of DNT)
	ARD =0.067 mg/kg bw			
Chronic Dietary	NOAEL = 8	Thyroid effects, decreased body weight gain, cholesterol changes	1 year - Dog; 2-year chronic / cancer study - Rat	1000 (10x for EDC and lack of DNT)
	ADI = 0.008 mg/kg bw/day			
Short-Term[a] Inhalation and Incidental Oral	Oral NOAEL = 10	Decreased body weight and food consumption	Developmental Toxicity - Rabbit	300
Short-Term[a] Dermal	Dermal NOAEL = 100	Decreased body weight and food consumption	21-day dermal - Rabbit	300
Intermediate[b] and Long-Term Dermal[c] and Inhalation[c]	NOAEL = 8	Thyroid effects, decreased body weight gain, cholesterol changes	1 year - Dog; 2-year chronic / cancer study - Rat	1000 (10x for EDC and lack of DNT)
Aggregate[c] (Oral, Dermal and Inhalation)	Oral and Inhalation NOAEL = 10 Dermal NOAEL = 100	Decreased body weight and food consumption	Developmental Toxicity - Rabbit; 21-day dermal - Rabbit	300
Cancer Q_1*		Liver tumours in male mice	18-month dietary carcinogenicity - Mice	1.32×10^{-2} $(mg/kg\ bw/day)^{-1}$

[a] Duration of exposure is >1-30 days
[b] Duration of exposure is 1-6 months
[c] A dermal absorption factor of 25% and an inhalation absorption factor of 100% was used in route-to-route extrapolation to an oral NOAEL.
DNT: Developmental Neurotoxicity Study
EDC: Endocring Disrupting Compound

Table 2 Toxicology endpoints for carbendazim health risk assessment

Exposure Scenario	Dose (mg/kg bw/day)	Endpoint	Study	UF or MOE
Acute Dietary Males	LOAEL = 50	Sperm effects	Acute oral - Rat	1000 (LOAEL, serious effect)
	ARD = 0.05 mg/kg bw			
Acute Dietary Females 13-49	NOAEL = 10	Fetal malformations, resorptions	Developmental Toxicity - Rat and Rabbit	1000 (sensitivity, serious effect, lack of DNT)
	ARD = 0.01 mg/kg bw			
Chronic Dietary	NOAEL = 9	Decreased body weight gain, biochemical parameters	2 year - Dog	1000 (sensitivity, serious effect, lack of DNT)
	ADI = 0.009 mg/kg bw/day			
Short-Term[a] and Intermediate-Term[b] Dermal[c] and Inhalation[c] & Aggregate[c] Oral, Dermal, and Inhalation for Females 13-49	Oral NOAEL = 10	Fetal malformations, resorptions	Developmental Toxicity - Rat and Rabbit	1000 (as above)
Aggregate[c] General Population (Oral and Inhalation)	Oral and Inhalation NOAEL = 20	Decreased body weight body weight gain	Developmental Toxicity - Rabbit, Rat	300 (sensitivity)
Cancer Q_1* (mg/kg bw/day)$^{-1}$		Liver tumours in female mice	2-year dietary carcinogenicity - Mice	1.6×10^{-2}

[a] Duration of exposure is >1-30 days
[b] Duration of exposure is 1-6 months
[c] A dermal absorption factor of 25% and an inhalation absorption factor of 100% was used in route-to-route extrapolation to an oral NOAEL.
DNT: Developmental Neurotoxicity Study

Appendix VI Occupational Exposure Risk Estimates for Thiophanate-methyl

Table 1 Dermal and inhalation MOEs for short-term mixing/loading and applying thiophanate methyl

Crop	Formu-lation	App Equip	application rate (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Dermal MOE [a]		Inhalation MOE [b]		Combined MOEs[c] (target = 300)		
					mid-level PPE[d]	maximum PPE[e]	w/out respirator	with respirator	mid-level PPE		maximum PPE
									w/out respirator	with respirator	with respirator
USC 4 Forests and Woodlots											
Aspen and Poplar	WSP	airblast	0.77	16	1147	1189	9501	95014	1023	1133	1174
		backpack	0.00077	150 L	23336	29894	97594	975943	18833	22791	29006
		LPH			82433	87380	134084	1340842	51049	77658	82034
		HPH		3750 L	988	1327	1605	16055	612	931	1226
		right-of-way sprayer			4557	5276	46800	468000	4153	4513	5217
USC 10 Seed Treatment Food and Feed											
Dry common Beans - on farm [f]	WP	M/L/A	0.73 g a.i./kg of seed	3000 kg of seed handled per day	397	NA	94268		396		NA
Sweet Corn - on farm [f]	WP	M/L/A	0.70 g a.i./kg of seed	1320 kg of seed handled per day	939	NA	222816		935		NA
Potatoes (cut seed) [g]	DU	Filling Duster	0.5 g a.i./kg of seed	10 000 kg of seed handled per day	538	NA	414	828 [i]	234	326	NA
		Cutting/ Sorting			6061	NA	8235	16471 [i]	3491	4430	NA
		Planting			8974	NA	10000	20000 [i]	4730	6195	NA

Crop	Formu-lation	App Equip	application rate (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Dermal MOE [a]		Inhalation MOE [b]		Combined MOEs[c] (target = 300)		
					mid-level PPE[d]	maximum PPE[e]	w/out respirator	with respirator	mid-level PPE		maximum PPE
									w/out respirator	with respirator	with respirator
USC 14 Terrestrial Food Crops											
Apples and Pears	WSP	airblast	0.438 (Eastern)	16	2018	2092	16722	167224	1801	1994	2066
			1.58 (Western)		559	579	4630	46304	499	552	572
Lowbush Blueberries	WSP	M/L for aircraft	0.77	200	5739	8775	25253	252525	4676	5612	6512 (no respirator)
		aircraft			4705	NA	64935	NA	4388	NA	NA
		groundboom		30	10464	12663	26582	265816	7508	10067	12087
		LPH	0.00077	150 L	82433	87380	134084	1340842	51049	77658	82034
		backpack			23336	29894	97594	975943	18833	22791	29006
Cherries, Nectarines, Plums, Prunes and Peaches	WSP	airblast	1.23	16	718	744	5948	59480	640	709	735
Raspberries and Strawberries	WSP	groundboom	0.77	30	10464	12663	26582	265816	7508	10067	12087
		LPH	0.00077	150 L	82433	87380	134084	1340842	51049	77658	82034
		backpack			23336	29894	97594	975943	18833	22791	29006
White Beans	WSP	groundboom	1.58	100	1535	1857	3899	38986	1101	1477	773
				300	512	619	1300	12995	367	492	591
		M/L for aircraft		400	1403	2145	6173	61728	1143	1372	2073
		aircraft			1150	NA	15873	NA	1073	NA	NA

Crop	Formu-lation	App Equip	application rate (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Dermal MOE [a]		Inhalation MOE [b]		Combined MOEs[c] (target = 300)		
					mid-level PPE[d]	maximum PPE[e]	w/out respirator	with respirator	mid-level PPE		maximum PPE
									w/out respirator	with respirator	with respirator
Sugar beets	WSP	groundboom	0.39	30	20659	25002	52482	524816	14824	19877	23865
USC 27 Ornamental outdoor											
Outdoor Ornamentals and Roses (commercial)	WSP	LPH	0.00053	150 L	120901	128158	196657	1966568	74871	113899	120317
		backpack			34226	43845	143138	1431383	27622	33427	42542
		HPH		3750 L	1449	1946	2355	23547	897	1365	1797
		groundboom	0.525	30	15347	18573	38986	389864	11012	14766	17728
		airblast		16	1682	1743	13935	139353	1501	1662	1722
USC 30 Turf											
Golf Course	Gr	push rotary spreader [h]	3	2	8642	NA	7071	70707	3889	7701	NA
		tractor drawn spreader		16	11429	NA	3838	38377	2873	8806	NA
	WSP	low pressure turf gun [h]	12.25	2	613	NA	1970	19704	468	595	NA
	WSP	backpack		0.4	550	705	2300	23004	444	537	684
	WSP	groundboom		16	1233	1492	3133	31328	885	1187	1425

[a] Dermal MOE = dermal exposure/dermal NOAEL. The dermal NOAEL is 100 mg/kg body weight/day. The target dermal MOE is 300.
[b] Inhalation MOE = inhalation exposure/inhalation NOAEL. The inhalation NOAEL is 10 mg/kg body weight/day. The target inhalation MOE is 300. There is a protection factor of 90% for respirators
[C] Combined MOE = 1/((1/dermal MOE) + (1/inhalation MOE))
[d] Mid-level PPE = coveralls over single layer, chemical gloves with and without respirator. PPE not specified for on-farm potato seed treatment.
[e] Maximum PPE = chemical resistant coveralls over single layer, chemical gloves with a respirator
[f] Unit exposure numbers are from a published study (Fenske et al, 1990).
[g] Unit exposure numbers are from a published study (Stevens and Davis, 1981).
[h] The dermal and inhalation values are from the ORETF. For mid-level PPE, it is coveralls over long pants, long sleeves, gloves and with and without a respirator. For the maximum PPE, there is no data available.
[i] The respirator for this study was a dust/mist filtering respirator
NA: not applicable

Table 2 Dermal and inhalation MOEs for intermediate-term mixing/loading and applying thiophanate methyl

The following crops were assessed as intermediate-term exposure (1-6 months) even though the WSP product is now limited to 2 applications per crop per season. These longer term scenarios account for potential custom application or situations were one applicator may be treating more than one crop per season (i.e. indoor and outdoor ornamentals).

Crop	Formula-tion	Application Equipment	Application rate (kg a.i./ha or kg a.i./L)	Area treated per day (ha or L)	Dermal MOE[a]		Inhalation MOE[b]		Combined MOEs [c] (target = 1000)		
									Mid-level PPE		Max PPE
					mid-level PPE [d]	maximum PPE [e]	w/out respirator	w/ respirator	w/out respirator	w/ respirator	w/ respirator
USC 6 Greenhouse non-food crops											
Potted Ornamentals	WSP	backpack	0.000595	150 L	9664	12380	101039	1010388	8820	9572	12230
		LPH			34137	36186	138817	1388166	27399	33317	35266
		HPH		3750 L	409	549	1662	16621	328	399	532
		Drench	5.95	1.2 ha	39612	60565	435730	4357298	36311	39255	59734
USC 10 Seed Treatment Food and Feed											
Dry common Beans [f] - Commercial	WP	loader/ applicator-1	0.73 g a.i./kg of seed	68 000 kg of seed handled per day	892	NA	150916	1509157	887	892	NA
		loader/ applicator-2			1140	NA	150916	1509157	1132	1339	NA
		sewer			3310	NA	223093	2230928	3262	3306	NA
		bagger			2255	NA	320696	3206960	2240	2254	NA
		multiple activities			489	NA	32070	320696	481	488	NA

Crop	Formula-tion	Application Equipment	Application rate (kg a.i./ha or kg a.i./L)	Area treated per day (ha or L)	Dermal MOE[a]		Inhalation MOE[b]		Combined MOEs [c] (target = 1000)		
									Mid-level PPE		Max PPE
					mid-level PPE [d]	maximum PPE [e]	w/out respirator	w/ respirator	w/out respirator	w/ respirator	w/ respirator
Sweet Corn [f] - Commercial	WP	loader/ applicator-1	0.70 g a.i./ kg of seed	60 000 kg of seed handled per day	1052	NA	177879	1778794	1046	1051	NA
		loader/ applicator-2			1344	NA	177879	1778794	1334	1343	NA
		sewer			3902	NA	262952	2629521	3845	3896	NA
		bagger			2658	NA	377994	3779937	2640	2657	NA
		Multiple activities			576	NA	37799	377994	567	575	NA
USC 27 Ornamental outdoor											
Outdoor Ornamentals and Roses (commercial)	WSP	LPH	0.000525	150 L	38688	41010	157325	1573255	31052	37760	39969
		backpack			10952	14030	114511	1145106	9996	10849	13861
		HPH		3750 L	464	623	1884	18837	372	453	603
		groundboom	0.525	30	4911	5943	31189	300891	4243	4835	5832
		airblast		16	538	558	11148	11483	513	536	555
		airblast with headgear			NA	4029	11148	111483	NA	NA	2960 (no resp)
		airblast closed cab			5369	NA	87719	NA	5059	NA	NA

Crop	Formulation	Application Equipment	Application rate (kg a.i./ha or kg a.i./L)	Area treated per day (ha or L)	Dermal MOE[a]		Inhalation MOE[b]		Combined MOEs [c] (target = 1000)		
									Mid-level PPE		Max PPE
					mid-level PPE [d]	maximum PPE [e]	w/out respirator	w/ respirator	w/out respirator	w/ respirator	w/ respirator
USC 30 Turf											
Golf Course	GR	push rotary spreader [g]	3	2	2765	NA	5657	56566	1857	2637	NA
		tractor drawn spreader		16	3657	NA	3070	30702	1669	3268	NA

[a] Dermal MOE = dermal exposure/dermal NOAEL. The dermal NOAEL is 8 mg/kg body weight/day. The target dermal MOE is 1000.
[b] Inhalation MOE = inhalation exposure/inhalation NOAEL. The inhalation NOAEL is 8 mg/kg body weight/day. The target inhalation MOE is 1000.
[c] Combined MOE = 1/((1/dermal MOE) + (1/inhalation MOE))
[d] Mid-level PPE = coveralls over single layer, gloves with and without respirator (unique PPE for commercial seed treatment - see comment f)
[e] Maximum PPE = chemical resistant coveralls over single layer, gloves with a respirator
[f] The unit exposure values are from U.S. EPA Policy 14 and have unique PPE scenarios: single layer, no gloves is for sewer and bagger, single layer and gloves is for loader/applicator (1) and multiple activities and coveralls and gloves is for loader/applicator (2). Data is not available for wettable powder formulation (only wettable powder packaged in water soluble packets).
[g] The dermal and inhalation values are from the ORETF. For mid-level PPE, it is coveralls over long pants, long sleeves, gloves and with and without a respirator. For the maximum PPE, there is no data available.
NA: not applicable

Table 3 Occupational Thiophanate-methyl Cancer Mixing/Loading/Applying Risk Estimates

Crop	Formulation	App Equip	application rate [a] (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Frequency Exposure per year [b]	Cancer			
						mid-level PPE without respirator		maximum PPE w/ respirator [c]	
						LADD [d]	Cancer Risk [e]	LADD [d]	Cancer Risk [e]
USC 4 Forests and Woodlots									
Aspen and Poplar	WSP	right-of-way sprayer	0.00077	3750 L	3	2.34e-05	3 E-07	1.30e-05	2 E-07
		backpack		150 L		4.82e-06	6 E-08	2.32e-06	3 E-08
		LPH				1.55e-06	2 E-08	8.04e-07	1 E-08
		HPH		3750 L		1.30e-04	2 E-06	5.33e-05	7 E-07
		airblast	0.77	16		9.39e-05	1 E-06	5.79e-05	8 E-07

Crop	Formulation	App Equip	application rate [a] (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Frequency Exposure per year [b]	Cancer			
						mid-level PPE without respirator		maximum PPE w/ respirator [c]	
						LADD [d]	Cancer Risk [e]	LADD [d]	Cancer Risk [e]
USC 6 - Greenhouse non-food crops									
Potted Ornamentals	WSP	backpack	0.000595	150 L	30	3.73e-05	5 E-07	2.69e-05	4 E-07
	WSP	LPH				1.20e-05	2 E-07	9.32e-06	1 E-07
	WSP	HPH		3750 L		1.00e-03	1 E-05	6.18e-04	8 E-06
	WSP	Drench	5.95	1.2 ha		9.05e-06	1 E-07	5.50e-06	8 E-08
USC 10 Seed Treatment Food and Feed									
ON FARM [f]									
Dry common Beans - on farm	WP	M/L/A	0.73 g a.i./kg of seed	3000 kg of seed handled per day	1	8.64e-05	1 E-06	NA	NA
Sweet Corn - on farm	WP	M/L/A	0.70 g a.i./kg of seed	1320 kg of seed handled per day	1	3.65e-05	5 E-07	NA	NA
Potatoes (cut seed)	DU	Filling Duster	0.5 g a.i./kg of seed	10 000 kg of seed handled per day	10	8.01e-07	1 E-08	NA	NA
		Cutting/ Sorting				6.48e-08	9 E-10	NA	NA
		Planting				4.50e-08	6 E-10	NA	NA
COMMERCIAL [g]									
Dry common Beans - Commercial	WP	Loader/ Applicator-1	0.73 g a.i./kg of seed	68 000 kg of seed handled per day	60	7.80e-04	1 E-05	NA	NA
		Loader/ Applicator-2				6.20e-04	8 E-06	NA	NA
		Sewer				2.28e-04	3 E-06	NA	NA
		Bagger				3.12e-04	4 E-06	NA	NA
		Multiple activities				1.55e-03	2 E-05	NA	NA
Sweet Corn - Commercial	WP	Loader/ Applicator-1	0.70 g a.i./ kg of seed	60 000 kg of seed handled per day	60	6.62e-04	9 E-06	NA	NA
		Loader/ Applicator-2				5.26e-04	7 E-06	NA	NA
		Sewer				1.94e-04	3 E-06	NA	NA

Crop	Formulation	App Equip	application rate [a] (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Frequency Exposure per year [b]	Cancer			
						mid-level PPE without respirator		maximum PPE w/ respirator [c]	
						LADD [d]	Cancer Risk [e]	LADD [d]	Cancer Risk [e]
		Bagger				2.65e-04	3 E-06	NA	NA
		Multiple activities				1.32e-03	2 E-05	NA	NA
USC 14 Terrestrial Food Crops									
Apples and Pears	WSP	airblast	0.438 (Eastern)	16	4	7.12e-05	9 E-07	6.58e-05	9 E-07
			1.58 (Western)			2.57e-04	3 E-06	2.38e-04	3 E-06
Lowbush Blueberries	WSP	M/L for aircraft	0.77	200	30	1.95e-04	3 E-06	3.30e-05	2 E-06 (no resp)
		aircraft				2.25e-04	3 E-06	NA	NA
		groundboom		30	4	1.52e-05	2 E-07	1.10e-05	1 E-07
		LPH	0.00077	150 L		2.07e-06	3 E-08	1.61e-06	2 E-08
		backpack				6.43e-06	8 E-08	4.64e-06	6 E-08
Cherries, Nectarines, Plums, Prunes and Peaches	WSP	airblast	1.23	16	3	1.50e-04	2 E-06	1.39e-04	2 E-06
Sugar beets	WSP	groundboom	0.39	30	2	3.84e-06	5 E-08	2.79e-06	4 E-08
Raspberries and Strawberries	WSP	groundboom	0.77	30	4	1.52e-05	2 E-07	1.10e-05	1 E-07
		LPH	0.00077	150 L		2.07e-06	3 E-08	1.61e-06	2 E-08
		backpack				6.43e-06	8 E-08	4.64e-06	6 E-08
White Beans	WSP	groundboom (farmer)	1.58	100	2	5.17e-05	7 E-07	3.76e-05	5 E-07
		groundboom (custom)		300	30	2.32e-03	3 E-05	1.69e-03	2 E-05
				200		1.55e-03	2 E-05	1.13e-03	1 E-05
		M/L for aircraft		400		7.99e-04	1 E-05	5.46e-04	7 E-06 (no respirator)
		aircraft				9.19e-04	1 E-05	NA	NA

Crop	Formulation	App Equip	application rate [a] (kg a.i./ha or kg a.i./L)	area treated per day (ha or L)	Frequency Exposure per year [b]	Cancer			
						mid-level PPE without respirator		maximum PPE w/ respirator [c]	
						LADD [d]	Cancer Risk [e]	LADD [d]	Cancer Risk [e]
USC 27 Ornamental outdoor									
Outdoor Ornamentals and Roses (commercial)	WSP	LPH		150 L	30	1.06e-05	1 E-07	8.23e-06	1 E-07
		backpack				3.29e-05	4 E-07	2.37e-05	3 E-07
		HPH	0.000525	3750 L		8.83e-04	1 E-05	5.45e-04	7 E-06
		groundboom	0.525	30		7.75e-05	1 E-06	5.64e-05	7 E-07
		airblast		16		6.40e-04	8 E-06	5.92e-04	8 E-06
USC 30 - Turf									
Golf Courses	GR	push rotary spreader [h]	3	2	6	4.21e-05	6 E-07	NA	NA
		tractor drawn spreader	3	16	6	3.94e-05	5 E-07	NA	NA
	WSP	low pressure turf gun [h]	12.25	2	1	9.22e-05	1 E-06	NA	NA
		backpack		0.4		6.82e-05	9 E-07	NA	NA
		groundboom		16		3.21e-05	4 E-07	2.34e-05	3 E-07

[a] The application rate is the maximum rate.
[b] Typical exposure frequencies were used. If necessary, these can be refined based on product specific limitations (not for custom).
[c] All scenarios are with respirator except for MLA aircraft
[d] LADD = Lifetime Average Daily Dose
[e] Cancer Risk = LADD (mg/kg/bw/day) × Q_1* (0.0132)
[f] On farm seed treatment includes the use of a dust filter / respirator with the mid-level PPE
[g] The unit exposure values have unique PPE scenarios: single layer, no gloves is for sewer and bagger, single layer and gloves is for loader/applicator (1) and multiple activities and coveralls and gloves is for loader/applicator (2).
[h] The dermal and inhalation values are from the ORETF. For mid-level PPE, it is coveralls over long pants, long sleeves, gloves and with and without a respirator. For the maximum PPE, there is no data available.

Shaded cells indicate a cancer risk for workers (> $1x10^{-5}$).
A cancer risk less than or equal to 1×10^{-5} is considered acceptable for occupational scenarios.
Occupational cancer risk is less than $1x10^{-5}$ for all uses except:

- Dry common Beans - Commercial seed multiple activities
- Sweet corn - commercial seed multiple activities
- White Beans - M/L/A custom groundboom with maximum PPE

White beans groundboom scenario can be mitigated by limiting the area treated per day to 200ha, or by limiting the amount of thiophanate-methyl used per day to 315kg.

Commercial seed treatment cannot be mitigated or refined further without new data.

Table 4 Postapplication Non-Cancer Exposure Estimates, MOEs and REIs for Thiophanate Methyl

Activity	Transfer Coefficient [a] (cm²/hr)	Short-Term (Target = 300)				Intermediate-Term (Target = 1000)			
		SRL [b] µg/cm²	Dermal Exposure [c] (µg/kg bw/day)	MOE [d] day 0	Proposed REI [e]	SRL [b] µg/cm²	Dermal Exposure [c] µg/kg bw/day	MOE [d] day 0	Proposed REI [e]
Lowbush Blueberries (0.77 kg a.i./ha)									
irrigate, scout, thin	400	7.29	3.06	715	0	NA	NA	NA	NA
hand harvest, prune	1500	1.94	3.06	**191**	1	NA	NA	NA	NA
Raspberries (0.77 kg a.i./ha)									
hand weed, irrigate, scout	500	5.83	174.84	572	0	NA	NA	NA	NA
hand harvest, prune, thin, train, tie	1500	1.94	524.57	**191**	1	NA	NA	NA	NA
Strawberries (0.77 kg a.i./ha)									
irrigate, mulch, hand weed, scout, thin	400	7.29	139.89	715	0	NA	NA	NA	NA
hand harvest, pinch, prune, train	1500	1.94	524.57	**191**	1	NA	NA	NA	NA
White Beans (1.58 kg a.i./ha)									
hand weed	100	29.17	71.54	1398	0	NA	NA	NA	NA
irrigate, scout	1500	1.94	1073.14	**93**	2	NA	NA	NA	NA
hand harvest	2500	1.17	1788.57	**56**	3	NA	NA	NA	NA
Sugar beets (0.39 kg a.i./ha)									
thin, hand weed	100	29.17	17.71	5645	0	NA	NA	NA	NA
irrigate, scout	1500	1.94	265.71	376	0	NA	NA	NA	NA
Apples and Pears (1.58 kg a.i./ha - Western) (BASED ON NY DATA)									
weed, prop	100	29.17	41.13	243	0	NA	NA	NA	NA

Activity	Transfer Coefficient [a] (cm²/hr)	Short-Term (Target = 300)				Intermediate-Term (Target = 1000)			
		SRL [b] µg/cm²	Dermal Exposure [c] (µg/kg bw/day)	MOE [d] day 0	Proposed REI [e]	SRL [b] µg/cm²	Dermal Exposure [c] µg/kg bw/day	MOE [d] day 0	Proposed REI [e]
prune, scout, pinch, tie, train	500	5.83	205.67	486	0	0.56	51.42	**156**	11
hand harvest	1500	1.94	617	**162**	4	NA	NA	NA	NA
thin	3000	0.97	1234.11	**81**	8	NA	NA	NA	NA
Apples and Pears (0.4375 kg a.i./ha - Eastern) (BASED ON NY DATA)									
weed, prop	100	29.17	11.39	8780	0	NA	NA	**NA**	NA
prune, scout, pinch, tie, train	500	5.83	56.95	1756	0	0.56	14.71	**562**	4
hand harvest	1500	1.94	170.85	585	0	NA	NA	NA	NA
thin	3000	0.97	341.69	**293**	1	NA	NA	NA	NA
Peaches, Nectarines, Plums, Prunes and Cherries (1.23 kg a.i./ha) (BASED ON NY DATA)									
weed, prop	100	29.17	32.02	3123	0	NA	NA	NA	NA
prune, scout, pinch, tie, train	500	5.83	160.11	625	0	0.56	40.03	**200**	9
hand harvest	1500	1.94	480.32	208	3	NA	NA	NA	NA
thin	3000	0.97	960.65	104	6	NA	NA	NA	NA
Aspen and Poplar (0.77 kg a.i./ha) (BASED ON NY DATA)									
hand prune, scout, pinch, tie, train	500	5.83	100	1000	0	NA	NA	NA	NA
hand-line irrigate	1100	2.65	220	455	0	NA	NA	NA	NA

Activity	Transfer Coefficient [a] (cm²/hr)	Short-Term (Target = 300)				Intermediate-Term (Target = 1000)			
		SRL [b] µg/cm²	Dermal Exposure [c] (µg/kg bw/day)	MOE [d] day 0	Proposed REI [e]	SRL [b] µg/cm²	Dermal Exposure [c] µg/kg bw/day	MOE [d] day 0	Proposed REI [e]
Roses and Ornamental Plants Outdoor (0.525 kg a.i./ha)									
All activities (excluding cut flowers)	400	NA	NA	NA	NA	0.7	23.84	**336**	2
cut roses	4000	NA	NA	NA	NA	0.07	238.42	**34**	5
Greenhouse Potted Ornamentals (0.595 kg a.i./ha) (2 applications, DFR based on greenhouse study with roses and mums)									
All activities for potted ornamentals	400	NA	NA	NA	NA	0.7	21.38	**374**	20
Turf (based on CA turf study predicted TTR)									
scout, irrigate, aerate 3 kg a.i./ha	500	5.83	11.25	8887	0	0.56	2.81	**2844**	0
scout, irrigate, aerate 4.2 kg a.i./ha	500	5.83	15.75	6348	0	0.56	3.94	**2031**	0
scout, irrigate, aerate 12.25 kg a.i./ha	500	5.83	45.95	2176	0	NA	NA	NA	NA
mowing [f] and misccellaneous 3 kg a.i./ha	3500	2.22	29.54	3386	0	0.21	7.38	**1083**	0
mowing [f] and misccellaneous 4.2 kg a.i./ha	3500	2.22	41.35	2418	0	0.21	3.94	**774**	1
mowing [f] and misccellaneous 12.25 kg a.i./ha	3500	2.22	120.61	829	0	NA	NA	NA	NA

[a] Transfer coefficients are from the Science Advisory Council for Exposure Agricultural Transfer Coefficient document (Revised - August 7, 2000) and any amendments thereof.
[b] Safe Residue Limit (SRL) = DFR/TTR represent the value at the day of safe re-entry (proposed REI)
[c] Dermal exposure at Day 0 = DFR × TC × 8 hr / 70 kg.
[d] Based on the short-term dermal NOAEL of 100 mg/kg/day and a target MOE of 300. Based on the intermediate-term dermal NOAEL of 8 mg/kg/day and a target MOE of 1000.
[e] The proposed REI in order reach a target MOE of 300 for short-term and 1000 for intermediate term post application exposure scenarios
[f] Mowing times were reduced to 3 hours per day based on public comments regarding the use of TPM on golf courses.

Table 5 Postapplication Non-Cancer Occupational Exposure Estimates and MOEs for Carbendazim

Activity	Transfer Coefficient (cm^2/hr) [a]	Proposed REI [b]	15% of the DFR/TTR value at the proposed REI [c]	Dermal Exposure [d] (mg/kg/day)	CAZ Short/ Intermediate-Term MOE [e] target = 1000	CAZ Long-Term MOE [f] target = 1000
Lowbush Blueberries (0.77 kg a.i./ha)						
irrigate, scout, thin, prune	400	0	0.459	0.00523	1906	NA
hand harvest, prune	1500	1	0.219	0.00939	1065	NA
Raspberries (0.77 kg a.i./ha)						
weed, irrigate, scout	500	0	0.459	0.00656	1525	NA
hand harvest, prune, thin, train, tie	1500	1	0.219	0.00939	1066	NA
Strawberries (0.77 kg a.i./ha)						
irrigate, mulch, weed, scout, thin	400	0	0.459	0.00525	1907	NA
hand harvest, pinch, prune, train	1500	1	0.219	0.00938	1066	NA
White Beans (1.58 kg a.i./ha)						
weed	100	0	0.9388	0.00268	3728	NA
irrigate, scout	1500	2	0.2137	0.00916	1092	NA
hand harvest	2500	3	0.1019	0.00728	1374	NA
Sugar beets (0.39 kg a.i./ha)						
thin, weed	100	0	0.2324	0.00066	15063	NA
irrigate, scout	1500	0		0.00996	1004	NA
Apples and Pears (BC rate 1.58 kg a.i./ha) Based on NY study site						
weed, prop	100	0	0.5399	0.00154	6483	NA
prune, scout, pinch, tie, train	500	11	0.0755	0.00108	9268	NA
hand harvest	1500	4	0.2641	0.0113	884	NA

Activity	Transfer Coefficient (cm^2/hr) [a]	Proposed REI [b]	15% of the DFR/TTR value at the proposed REI [c]	Dermal Exposure [d] (mg/kg/day)	CAZ Short/ Intermediate-Term MOE [e] target = 1000	CAZ Long-Term MOE [f] target = 1000
hand harvest (increased REI)	1500	5	0.2208	0.00946	1057	NA
thin	3000	8	0.1291	0.0111	903	NA
thin (increased REI)	3000	9	0.108	0.00926	1080	NA
Apples and Pears (Eastern Provinces rate 0.4375 kg a.i./ha) Based on NY study site						
weed, prop	100	0	0.1495	0.00043	23413	NA
prune, scout, pinch, tie, train	500	4	0.0731	0.00104	9575	NA
hand harvest	1500	0	0.1495	0.00641	1561	NA
thin	3000	1	0.125	0.0101	933	NA
thin (increased REI)	3000	2	0.1045	0.00896	1116	NA
Peaches, Nectarines, Plums, Prunes and Cherries (1.23 kg a.i./ha) Based on NY study site						
weed, prop	100	0	0.4203	0.0012	8328	NA
prune, scout, pinch, tie, train	500	9	0.0841	0.0012	8326	NA
hand harvest	1500	3	0.2458	0.0105	949	NA
hand harvest (increased REI)	1500	4	0.2056	0.00881	1135	NA
thin	3000	6	0.1438	0.0123	812	NA
thin (increased REI)	3000	8	0.1005	0.00862	1160	NA
Aspen and Poplar (0.77 kg a.i./ha) Based on NY study site						
hand prune, scout, pinch, tie, train	500	0	0.2631	0.00376	2661	NA
hand-line irrigate	1100	0		0.00827	1209	NA
Roses and Ornamental Plants Outdoor (0.525 kg a.i./ha)						
All activities (excludes cut flowers)	400	2	0.0712	0.00081	12286	NA
cut roses	4000	5	0.0077	0.00088	11316	NA

Activity	Transfer Coefficient (cm^2/hr) [a]	Proposed REI [b]	15% of the DFR/TTR value at the proposed REI [c]	Dermal Exposure [d] (mg/kg/day)	CAZ Short/ Intermediate-Term MOE [e] target = 1000	CAZ Long-Term MOE [f] target = 1000
Greenhouse Potted Ornamentals (0.595 kg a.i./ha) DFR based on highest reported value from cut flower study (0.35 µg/cm^2) corrected for rate.						
All activities (excludes cut flowers)	400	20	0.1026	0.00117	NA	7672
Turf (Based on predicted TTR from CA study site)						
scout, irrigate, aerate - 12.25 kg a.i./ha	500	0	0.1206	0.00065	15477	NA
mowing - 12.25 kg a.i./ha	3500	1		0.00452	2211	NA
scout, irrigate, aerate - 3 kg a.i./ha	500	0	0.0414	0.00059	16928	NA
mowing - 3 kg a.i./ha	3500	1	0.0252	0.00095	10572	NA

a Transfer coefficients are from the Science Advisory Council for Exposure Agricultural Transfer Coefficient document (Revised - August 7, 2000) and any amendments thereof.
b Proposed REI is based on TPM non-cancer exposure as per Table 6.
c The residue level which results in an acceptable MOE for TPM; 15% of this value is estimated to be the amount of CAZ at the time of re-entry.
d Dermal exposure at proposed REI or when SRL reached = DFR × TC × 8 hr × DAF (25%) / 70 kg.
e Intermediate-term oral NOAEL of 10 mg/kg/day, dermal absorption factor of 25% and target MOE of 300.
f Long-term oral NOAEL of 9 mg/kg/day, dermal absorption factor of 25% and target MOE of 1000.

Non-cancer post application exposure was assessed for carbendazim. Based on the uncertainties in the percentage of thiophanate-methyl that degrades to carbendazim at any time in the environment, a default of 15% was selected to apply to the DFR/TTR data of thiophanate-methyl. Since postapplication thiophanate-methyl exposure results in REIs being proposed, the DFR/TTR residue data on the day of the proposed REI for thiophanate-methyl is used in the carbedazim risk assessment. If necessary, the REI was increased until the carbendazim risk was acceptable.

Most scenarios are based on short-term exposure for orchards, except scouting activities, which are based on intermediate term exposure. Therefore their proposed REI is the largest despite their lower TC.

Table 6 Postapplication Cancer Risk Estimates for Thiophanate-Methyl and Carbendazim

Activity	Transfer Coefficient (cm^2/hr)	Exposure Frequency[a] (days/year)	DFR/TTR[b] (average residues for TPM)	Thiophanate methyl			Carbendazim		
				Absorbed daily dermal dose (mg/kg/day)	LADD[c] (mg/kg/day)	Cancer Risk[d]	Absorbed daily dermal dose[e] (mg/kg/day)	LADD[c] (mg/kg/day)	Cancer Risk[f]
Lowbush Blueberries (0.77 kg a.i./ha) (DFR average of days 1-7)									
irrigate, scout, thin, prune	400	30	0.3965	0.0045	1.86e-04	2 E-06	0.00068	2.79e-05	4 E-07
hand harvest, prune	1500	30		0.017	6.98e-04	9 E-06	0.00255	1.05e-04	2 E-06
Raspberries (0.77 kg a.i./ha) (DFR average of days 1-7)									
weed, irrigate, scout	500	30	0.3965	0.0057	2.33e-04	3 E-06	0.00085	3.49e-05	6 E-07
hand harvest, prune, thin, train, tie	1500	30		0.017	6.98e-04	9 E-06	0.00255	1.05e-04	2 E-06
Strawberries (0.77 kg a.i./ha) (DFR average of days 1-7)									
irrigate, mulch, weed, scout, thin	400	30	0.3965	0.0045	1.86e-04	2 E-06	0.00068	2.79 E-05	4 E-0 7
hand harvest, pinch, prune, train	1500	30		0.017	6.98e-04	9 E-06	0.00255	1.05e-04	2 E-06
White Beans (1.58 kg a.i./ha) (Refined DFR averages [h])									
weed	100	30	0.811	0.0023	9.52e-05	1 E-06	0.000348	1.43e-05	2 E-07
irrigate, scout	1500	30	0.4486	0.0192	7.90e-04	1 E-05	0.00521	2.14e-04	3 E-06
hand harvest	2500	30	0.2535	0.0181	7.44e-04	1 E-07	0.00869	3.57e-04	6 E-06
Sugar beets (0.39 kg a.i./ha) (DFR average of days 1-7)									
thin, weed	100	30	0.2	0.0006	2.36e-05	3 E-07	0.0000861	3.54e-06	6 E-08
irrigate, scout	1500	30		0.0086	3.54e-04	5 E-06	0.00129	5.31e-05	8 E-07

Activity	Transfer Coefficient (cm²/hr)	Exposure Frequency[a] (days/year)	DFR/TTR[b] (average residues for TPM)	Thiophanate methyl			Carbendazim		
				Absorbed daily dermal dose (mg/kg/day)	LADD[c] (mg/kg/day)	Cancer Risk[d]	Absorbed daily dermal dose[e] (mg/kg/day)	LADD[c] (mg/kg/day)	Cancer Risk[f]
Apples and Pears (1.58 kg a.i./ha) - BC only (based on NY data) (Refined DFR averages [i])									
weed, prop	100	30	0.6099	0.0017	7.16e-05	9 E-07	0.000261	1.07e-05	2 E-07
prune, scout, pinch, tie, train	500	60	0.6099	0.0087	7.16e-04	9 E-06	0.00131	1.07e-04	2 E-06
hand harvest	1500	30	0.3425	0.0147	6.03e-04	8 E-06	0.00392	1.61e-04	3 E-06
thin	3000	30	0.196	0.0168	6.90e-04	9 E-06	0.00784	3.22e-04	5 E-06
Apples and Pears (0.4375 kg a.i./ha) - Eastern Provinces (based on NY data) (DFR average of days 1 - 30)									
weed, prop	100	30	0.1689	0.0005	1.98e-05	3 E-07	0.0000724	2.97e-06	5 E-08
prune, scout, pinch, tie, train	500	60	0.1689	0.0024	1.98e-04	3 E-06	0.000362	2.97e-05	5 E-07
hand harvest	1500	30	0.1689	0.0072	2.97e-04	4 E-06	0.00109	4.46e-05	7 E-07
thin	3000	30	0.1689	0.0145	5.95e-04	8 E-06	0.00217	8.92e-05	1 E-06
Peaches, Nectarines, Plums, Prunes and Cherries (1.23 kg a.i./ha) (based on NY data) (Refined DFR averages [j])									
weed, prop	100	30	0.4748	0.0014	5.58e-05	7 E-07	0.000203	8.36e-06	1 E-07
prune, scout, pinch, tie, train	500	45	0.4748	0.0068	4.18e-04	6 E-06	0.00102	6.27e-05	1 E-06
hand harvest	1500	30	0.3075	0.0132	5.42e-04	7 E-06	0.00305	1.25e-04	2 E-06
thin	3000	30	0.1751	0.015	6.17e-04	8 E-06	0.0061	2.51e-04	4 E-06
Aspen and Poplar (0.77 kg a.i./ha) (based on NY data) (DFR average of days 1-30)									
hand prune, scout, pinch, tie, train	500	30	0.2972	0.0042	1.75e-04	2 E-06	0.000637	2.62e-05	4 E-07
hand-line irrigate	1100			0.0093	3.84e-04	5 E-06	0.0014	5.76e-05	9 E-07

Activity	Transfer Coefficient (cm²/hr)	Exposure Frequency[a] (days/year)	DFR/TTR[b] (average residues for TPM)	Thiophanate methyl			Carbendazim		
				Absorbed daily dermal dose (mg/kg/day)	LADD[c] (mg/kg/day)	Cancer Risk[d]	Absorbed daily dermal dose[e] (mg/kg/day)	LADD[c] (mg/kg/day)	Cancer Risk[f]
Roses and Ornamental Plants Outdoor (0.525 kg a.i./ha) (Refined DFR averages [k])									
All activities (ornamentals)	400	90	0.27	0.0031	3.81e-04	5 E-06	0.000463	5.71e-05	9 E-07
All activities (cut flowers)	4000	90	0.0293	0.0176	4.13e-04	5 E-06	0.00463	5.71e-04	9 E-06
Greenhouse Potted Ornamentals (0.595 kg a.i./ha) (DFR average of days 1-7)									
All activities (potted ornamentals)	400	90	1.5381	0.0176	2.17e-01	3 E-05	0.00264	3.25e-04	5 E-06
Turf (3 kg a.i./ha) (based on CA residue study) (TTR average of days 1-7)									
scout, irrigate, aerate	500	60	0.0426	0.0006	5.00e-05	7 E-07	0.0000913	1.13e-05	2 E-07
mowing [g]	3500	60		0.0016	1.31e-04	2 E-06	0.00024	1.58e-05	5 E-07
Turf (4.2 kg a.i./ha) (based on CA residue study) (TTR average of days 1-7)									
scout, irrigate, aerate	500	60	0.0597	0.0009	7.01e-05	9 E-07	0.000128	1.58e-05	3 E-07
mowing [g]	3500	60		0.0022	1.84e-04	2 E-06	0.000336	4.14e-05	7 E-06

[a] Based on information from the U.S. EPA RED for TPM and PMRA refinements.
[b] Based on the average DFR/TTR data as described in the table.
[c] Lifetime average daily dose, amortising 35 years of occupational exposure over a 70-year lifetime for workers.
[d] Cancer Risk = LADD (mg/kg/day) × Q^* (0.0132)
[e] Based on 15% of the average estimated residues of TPM; includes incorporating a dermal absorption factor of 25%,
[f] Cancer Risk = LADD (mg/kg/day) × Q^* (0.016)
[g] Mowing times were reduced to 3hours per day based on public comments regarding the use of TPM on golf courses.
[h] White bean DFR average was refined for TPM as follows: hand weeding (DFR average of days 1-7); irrigation, scouting (DFR average of days 2-7); hand harvesting (DFR average of days 3-7). However it remains as an average of days 1-7 for CAZ
[i] Apples and pears (BC rate) DFR average was refined as follows: weeding, propping, pruning, scouting, pinching, tying, and training (DFR average of days 1-30); hand harvesting (DFR average of days 5-30); hand thinning (DFR average of days 9-30). However it remains as an average of days 1-30 for CAZ
[j] Peaches, nectarines, plums, prunes and cherries DFR average was refined as follows: weeding, propping, pruning, scouting, pinching, tying, and training (DFR average of days 1-30); hand harvesting (DFR average of days 4-30); hand thinning (DFR average of days 8-30). However it remains as an average of days 1-30 for CAZ
[k] Outdoor roses and ornamental plants DFR average was refined as follows: all activities with ornamentals (DFR average of days 1-7); all activities with cut flowers (DFR average of days 5-7). However it remains as an average of days 1-30 for CAZ

A cancer risk less than or equal to 1×10^{-5} is considered acceptable for occupational scenarios.

Occupational postapplication cancer risk for thiophanate-methyl and carbendazim separately is less than $1x10^{-5}$ for all uses except:
- greenhouse potted ornamentals (all activities)

The greenhouse potted ornamental risk assessment cannot be refined further without new data. The assessment is considered refined as it is based on refined TC's and a greenhouse DFR study. However, the greenhouse potted ornamental risk assessment assumes foliar contact during the pesticide application process. If a drench application can be applied without any contact with the foliage of the potted ornamentals there will be very little dermal postapplication exposure during regular activities. Therefore the drench application can remain on the label, with a restriction limiting all foliar contact (i.e. no overhead drenching application).

Table 7 Postapplication Combined Cancer Risk Estimates for Thiophanate-methyl and Carbendazim

Cancer risk assessments for thiophanate-methyl and carbendazim need to be combined to determine if there are risk concerns. Carbendazim risk assessment is based on the assumption that 15% of thiophanate-methyl residues degrade to carbendazim. In order to avoid double counting, only 85% of the thiophanate-methyl cancer risk is combined with the carbendazim cancer risk. As carbendazim is more toxic than thiophanate-methyl, this is not expected to underestimate risk.

Activity	Transfer Coefficient (cm^2/hr)	Exposure Frequency (days/year)	TPM Cancer Risk[a]	CAZ Cancer Risk[b]	Combined Cancer Risk[c]
Lowbush blueberries					
irrigate, scout, thin, prune	400	30	2 E-06	4 E-07	3 E-06
hand harvest, prune	1500	30	9 E-06	2 E-06	1 E-07
Sugarbeets					
thin, weed	100	30	3 E-07	6 E-08	3 E-07
irrigate, scout	1500	30	5 E-06	9 E-07	5 E-06
Aspen and Poplar					
hand prune, scout, pinch, tie, train	500	30	2 E-06	4 E-07	2 E-06
hand-line irrigate	1100	30	5 E-06	9 E-07	5 E-06
Apples and Pears (BC only)					
weed, prop	100	30	9 E-07	2 E-07	0
prune, scout, pinch, tie, train	500	60	9 E-06	2 E-06	1 E-05
hand harvest	1500	30	8 E-06	3 E-06	9 E-06
thin	3000	30	9 E-06	5 E-06	1 E-05
Apples and Pears (Eastern Provinces)					
weed, prop	100	30	3 E-07	5 E-08	3 E-07
prune, scout, pinch, tie, train	500	60	3 E-06	5 E-07	3 E-06
hand harvest	1500	30	4 E-06	7 E-07	4 E-06

Activity	Transfer Coefficient (cm^2/hr)	Exposure Frequency (days/year)	TPM Cancer Risk[a]	CAZ Cancer Risk[b]	Combined Cancer Risk[c]
thin	3000	30	8 E-06	1 E-06	8 E-06
Peaches, nectarines, plums, prunes and cherries					
weed, prop	100	30	7 E-07	1 E-07	8 E-07
prune, scout, pinch, tie, train	500	60	6 E-06	1 E-06	6 E-06
hand harvest	1500	30	7 E-06	2 E-06	8 E-06
thin	3000	30	8 E-06	4 E-06	1 E-05
Raspberries					
weed, irrigate, scout	500	30	3 E-06	6 E-07	3 E-06
hand harvest, prune, thin, train, tie	1500	30	9 E-06	2 E-06	1 E-07
Strawberries					
irrigate, mulch, weed, scout, thin	400	30	2 E-06	4 E-07	3 E-06
hand harvest, pinch, prune, train	1500	30	9 E-06	2 E-06	1 E-07
White beans					
weed	100	30	1 E-06	2 E-07	1 E-06
irrigate, scout	1500	30	1 E-05	3 E-06	1 E-05
hand harvest	2500	30	1 E-07	6 E-06	1 E-05
Roses and ornamental plants outdoors					
All activities (ornamentals)	400	90	5 E-06	9 E-07	5 E-06
All activities (cut flowers)	4000	90	5 E-06	9 E-06	1 E-05
Greenhouse Potted Ornamentals (foliar application)					
All activities (potted ornamentals)	400	90	3 E-05	5 E-06	3 E-05
Turf Wettable Powder (4.2 kg a.i./ha)					
scout, irrigate, aerate	500	60	9 E-07	3 E-07	1 E-06
mowing	3500	60	2 E-06	7 E-07	3 E-06
Turf granular (3 kg a.i./ha)					
scout, irrigate, aerate	500	60	7 E-07	2 E-07	7 E-07
mowing	3500	60	2 E-06	5 E-07	2 E-06

[a] TPM Cancer Risk = LADD (mg/kg/day) × Q^* (0.0132); based on 50 years of exposure over a 70-year lifetime for adults
[b] CAZ Cancer Risk = LADD (mg/kg/day) × Q^* (0.016); based on 50 years of exposure over a 70-year lifetime for adults
[c] Combined TPM and CAZ Cancer Risk = (0.85TPM cancer risk) + CAZ cancer risk. 85% of TPM is counted to avoid double counting since CAZ is assumed to be 15% of TPM

A cancer risk less than or equal to 1×10^{-5} is considered acceptable for occupational scenarios.

Occupational postapplication cancer risk for thiophanate-methyl and carbendazim combined is less than 1×10^{-5} for all uses except:
- greenhouse potted ornamentals foliar application (all activities)

Appendix VII Non-Occupational Exposure and Risk Assessment

Table 1 summarizes M/L/A non-cancer and cancer risk estimates for residential application of dust formulation to roses, flowers, ornamentals and junipers. Exposure was calculated assuming a homeowner has short term exposure (<30 days) and uses a maximum of 1 can of product per day. The can is 300 g with a guarantee of 3% thiophanate-methyl. Therefore, the amount of active ingredient handled per day is 9 grams. The homeowner is assumed to be wearing short pants, short sleeved shirt and no gloves.

Residential cancer risk for this product is based on 3 applications per year for 50 years. A cancer risk less than or equal to 1×10^{-6} is considered acceptable for residential scenarios.

Table 1 Residential M/L/A Short -term and Cancer Risk Estimates

Equipment Type	Short-Term MOE (target MOE = 300)			LADD	Cancer Risk [d]
	Dermal [a]	Inhalation [b]	Combined [c]		
Shaker can / Squeeze container	2194	28690	2038	0.000113	1 E-06

a Dermal MOE = NOAEL (100 mg/kg/day) / Daily Dermal Dose (mg/kg/day). Dermal NOAEL from a dermal study, therefore, no adjustment for dermal absorption.
b Inhalation MOE = NOAEL (10 mg/kg/day) / Daily Inhalation Dose (mg/kg/day).
c Combined MOE = 1/(1/MOE dermal + 1/MOE inhalation).
d Cancer Risk = LADD (mg/kg/day) × Q*(0.0132)

This dust product has acceptable risk if use is limited to 3 times per year. A label statement will need to be added to ensure that use is limited to 3 times per year because additional applications resulted in unacceptable cancer risk.

Residential Postapplication Exposure Risk Estimates and Cancer Risk

The gardener scenario applies to a homeowner who has ornamentals, e.g. rose bushes, treated with 3 applications per year, 7 days apart, of thiophanate methyl at a rate of 1 kg a.i./ha, and who performs gardening activities for 40 minutes beginning on the day after application, and does so in this manner every year for 50 years over a 70 year lifespan. It is also based on the average DFR values from the strawberry DFR study (North Carolina site) from Day 1 to Day 7. This is considered a refined estimate.

The golfer cancer scenario is based on one application to a golf course at the typical rate of 4.2 kg a.i./ha and the granular rate of 3 kg a.i./ha, and that a golfer is exposed 5 times a year for 4 hours within 7 days of application, and does so in this manner every year for 20 years over a 70-year lifespan. It is also based on the average TTR values from the TTR study (Georgia site) from Day 1 to Day 7. This is considered a refined estimate. Risk estimates were also refined for youth golfers by correcting the transfer coefficient for body weight (344 cm^2/hr instead of 500cm^2/hr).

Table 2 Youth and Adult Postapplication Exposure and Cancer Risk for TPM in Residential Gardening and Golfing

Scenario	Transfer Coefficient (cm^2/hr)	Duration (hr)	DFR/TTR[a] at Day 0 (µg/cm^2)	DFR / TTR (Day 1-7 average)[b]	Dermal Exposure µg/kg bw/day at Day 0	Dermal MOE[c] at Day 0	LADD (mg/kg/day)	Cancer Risk[d] TPM
Gardeners (Roses, flowers and evergreens) Dust 1.0 kg a.i./ha						Target = 300		
Youth (39Kg)	2756 [e]	0.67	3.97	0.515	188	532	4.29e-06	6 E-08
Adult (70Kg)	4000				152	657	2.89e-05	4 E-07
Golfers (3.0 kg a.i./ha) Granular								
Youths (39 kg)	344 [e]	4	0.764	0.0818	27	3709	8.48e-07	1 E-08
Adult (70Kg)	500				22	4580	5.72e-06	8 E-08
Golfers (4.2 kg a.i./ha) WSB								
Youths (39 kg)	344 [e]	4	1.07	0.1146	38	2649	1.19e-06	2 E-08
Adult (70Kg)	500				31	3271	8.01e-06	1 E-07

[a] DFR value is based on predicted Day 0 value from a strawberry DFR study (NC site). TTR value based on highest reported TTR Day 0 value (PA study site Day 0.5 value).
[b] DFR value is based on the average predicted (Day 1 to Day 7) value from strawberry DFR study (North Carolina site). TTR value is based on the average predicted TTR (Day 1 to Day 7) value from the Georgia study site.
[c] Dermal MOE = NOAEL (100 mg/kg/day) / Daily Dermal Dose (mg/kg/day); target = 300
[d] Cancer Risk = LADD (mg/kg/day) × Q^* (0.0132); based on 50 years of exposure over a 70-year lifetime for adults (6 years for youth); exposure frequency of 3 days per year for gardeners and 5 days per year for golfers.
[e] Scaled for youth surface area (adult surface area=18440cm^2; youth surface area=12700cm^2).

Residential cancer risks from postapplication contact with treated ornamentals and turf, as shown in Table 2, are less than 1×10^{-6}.

Table 3 Youth and Adult Postapplication Exposure and Cancer Risk for Carbendazim in Residential Gardening and Golfing

Activity	Transfer Coefficient (cm^2/hr)	15% of DFR/TTR values of TPM at Day 0[a] (μg/cm^2)	15% of average Day 1-7 DFR/TTR of TPM (μg/cm^2)	Dermal Exposure[b] (mg/kg/day)	CAZ Short/ Intermediate-Term Dermal MOE[c]	Exposure Frequency (days/year)	LADD[d] (mg/kg/day)	CAZ Cancer Risk[e]
Turf (granular: 3 kg a.i./ha) (wettable powder: 4.2 kg a.i./ha)						**Target = 1000**		
golfing- youth 3 kg a.i./ha	344	0.1146	0.0123	0.00101	9890	5	1.27e-07	2 E-09
golfing- adult 3 kg a.i./ha	500			0.00082	12213	5	8.58e-07	1 E-08
golfing- youth 4.2 kg a.i./ha	344	0.1605	0.0172	0.00142	7064	5	1.38e-04	3 E-09
golfing- adult 4.2 kg a.i./ha	500			0.00115	8724	5	1.20e-06	2 E-08
Roses, Flowers and Evergreens Residential (1 kg a.i./ha)								
gardening activities-youth	2756	0.596	0.0772	0.00705	1417	3	6.44e-07	1 E-08
gardening activities-adult	4000			0.0057	1753	3	4.34e-06	7 E-08

a The highest percentage of TPM residues that degraded to CAZ is 15%.(PMRA 2005) For this reason, 15% of the DFR/TTR value of TPM at Day 0 was applied to obtain the CAZ DFRs/TTRs values.
b Non-cancer dermal exposure = DFR/TTR × TC × 4 hr (golfing) or 0.67 hr (gardening) × dermal absorption factor of 25%/ 70 kg for adults or 39 kg for youths.
c Based on the short/intermediate-term oral NOAEL of 10 mg/kg/day with a target MOE of 1000
d Lifetime average daily dose, amortising 50 years of non-occupational exposure over a 70-year lifetime for adults and 6 years over a 70-year lifetime for youth
e Cancer Risk = LADD (mg/kg/day) × Q^* (0.016)

The target MOE (1000) is met for both golfer and gardener postapplication non-cancer exposure scenarios. For cancer risk estimates, all residential postapplication scenarios were less than 1×10^{-6} .

Table 4 Youth and Adult Postapplication Exposure Combined Cancer Risk for TPM and Carbendazim in Residential Gardening and Golfing

Cancer risk assessments for thiophanate-methyl and carbendazim need to be combined to determine if the risk is acceptable. Carbendazim risk assessment is based on the assumption that 15% of thiophanate-methyl residues degrade to carbendazim. In order to avoid double counting, only 85% of the thiophanate-methyl cancer risk is combined with the carbendazim cancer risk. As carbendazim is more toxic than thiophanate-methyl, this is not expected to underestimate exposure.

Activity	Transfer Coefficient (cm^2/hr)	Exposure Frequency (days/year)	TPM Cancer Risk[a]	CAZ Cancer Risk[b]	Combined Cancer Risk[c]
Turf (granular: 3 kg a.i./ha) (wettable powder: 4.2 kg a.i./ha)					
golfing- youth 3 kg a.i./ha	344	5	1 E-08	2 E-09	1 E-08

Activity	Transfer Coefficient (cm^2/hr)	Exposure Frequency (days/year)	TPM Cancer Risk[a]	CAZ Cancer Risk[b]	Combined Cancer Risk[c]
golfing- adult 3 kg a.i./ha	500	5	8 E-08	1 E-08	8 E-08
golfing- youth 4.2 kg a.i./ha	344	5	2 E-08	3 E-09	2 E-08
golfing- adult 4.2 kg a.i./ha	500	5	1 E-07	2 E-08	1 E-07
Roses, Flowers and Evergreens Residential (1 kg a.i./ha)					
gardening activities-youth	2756	3	6 E-08	1 E-08	6 E-08
gardening activities-adult	4000	3	4 E-07	7 E-08	4 E-07

[a] TPM Cancer Risk = LADD (mg/kg/day) × Q^* (0.0132); based on 50 years of exposure over a 70-year lifetime for adults (6 years for youth); exposure frequency of 3 days per year for gardeners and 5 days per year for golfers

[b] CAZ Cancer Risk = LADD (mg/kg/day) × Q^* (0.016); based on 50 years of exposure over a 70-year lifetime for adults (6 years for youth); exposure frequency of 3 days per year for gardeners and 5 days per year for golfers

[c] Combined TPM and CAZ Cancer Risk = (0.85TPM cancer risk) + CAZ cancer risk

All residential postapplication scenarios have combined cancer (thiophanate-methyl and carbendazim) risks that are less than 1×10^{-6} .

Appendix VIII Dietary and Drinking Water Exposure Estimates for Thiophanate-Methyl and Carbendazim

Table 1 Dietary Exposure and Risk Estimates of Thiophanate-Methyl and Carbendazim

Population	Exposure (mg/kg bw/day)		Risk Estimates		
	Acute	Chronic	% ARfD	% ADI	Cancer
Thiophanate-Methyl					
Total Population[a]	N/A	0.000020	N/A	0.3%	5.5 × 10^{-7}
All infants (< 1 year)	0.00399	0.000047	3.07%	0.6%	
Children 1-2 years	0.00207	0.000072	1.60%	0.9%	
Children 3-5 years	0.00116	0.000051	0.89%	0.6%	
Children 6-12 years	0.00066	0.000026	0.51%	0.3%	
Youth 13-19 years	♂ 0.00051	♂&♀ 0.000012	0.32%	0.4%	
Adults 20-49 years	♂ 0.00029	♂&♀ 0.000012	0.22%	0.2%	
Adults 50+ years	0.00041	0.00002	0.32%	0.2%	
Females 13-49 years	0.00034	0.00001	0.50%	0.2%	
Reference Doses	ARfD	0.13	mg/kg bw		
	ARfD ♀ 13-50	0.067			
	ADI	0.008	mg/kg bw/day		
	Q_1*	0.0132	(mg/kg bw/day)$^{-1}$		
Carbendazim					
Total Population[a]	N/A	0.000018	N/A	0.2%	
All infants (< 1 year)	0.00316	0.000039	6.33%	0.4%	
Children 1-2 years	0.00163	0.000064	3.27%	0.7%	
Children 3-5 years	0.00120	0.000048	2.39%	0.5%	
Children 6-12 years	0.00064	0.000026	1.28%	0.3%	
Youth 13-19 years	♂ 0.00052	♂&♀ 0.000013	0.98%	1.0%	
Adults 20-49 years	♂ 0.00033	♂&♀ 0.000013	0.69%	0.7%	
Adults 50+ years	0.00034	0.000015	0.68%	0.2%	
Females 13-49 years	0.00036	0.000013	3.57%	0.1%	
Reference Doses	ARfD	0.05	mg/kg bw		
	ARfD ♀ 13-50	0.01			
	ADI	0.009	mg/kg bw/day		
	Q_1*	0.016	(mg/kg bw/day)$^{-1}$		

ARfD = Acute Reference Dose; ADI = Acceptable Daily Intake.

[a] The risk estimate could not be determined for the general population as a separate ARfD was selected for females aged 13-49 years and the other population groups.

Table 2 Thiophanate-Methyl Drinking Water Concentrations Estimated from Models and Monitoring Data

	Groundwater Concentration (µg/L)		Surface-Water Acute Concentration (µg/L)		Surface-Water Chronic Concentration (µg/L)	
	Acute	**Chronic**	**Reservoir**	**Dugout**	**Reservoir**	**Dugout**
Upper Bound [1]	0.00 [3]	0.00 [4]	56 [5]	NA [6]	3.4 [7]	NA [6]
Lower Bound [2]	NA	NA	NA		NA	

NA = Not Available
1 Upper Bound concentrations are from modelling results
2 Lower Bound concentrations are from monitoring data, which were not available
3 90th percentile of the daily average concentrations, Level 2 modelling
4 90th percentile of the annual average concentrations, Level 2 modelling
5 90th percentile of the annual peak concentrations, Level 2 modelling
6 Use in the Prairies was not considered, which eliminated the dugout
7 90th percentile of the annual average concentrations, Level 2 modelling

Table 3 Carbendazim Drinking Water Concentrations Estimated from Models and Monitoring Data (with a 0.827 conversion factor*)

	Groundwater Concentration (µg/L)		Surface-Water Acute Concentration (µg/L)		Surface-Water Chronic Concentration (µg/L)	
	Acute	**Chronic**	**Reservoir**	**Dugout**	**Reservoir**	**Dugout**
Upper Bound [1]	3.47 [3]	3.47 [4]	27.29 [5]	NA [6]	9.1 [7]	NA [6]
Lower Bound [2]	NA	NA	NA		NA	

NA = Not Available
1 Upper Bound concentrations are from modelling results
2 Lower Bound concentrations are from monitoring data, which were not available
3 90th percentile of the daily average concentrations, Level 2 modelling
4 90th percentile of the annual average concentrations, Level 2 modelling
5 90th percentile of the annual peak concentrations, Level 2 modelling
6 Use in the Prairies was not considered, which eliminated the dugout
7 90th percentile of the annual average concentrations, Level 2 modelling
*The maximum conversion of TM to MBC of 0.827 based on results from the aerobic soil metabolism study

Table 4 Acute, Chronic and Cancer Drinking Water Levels of Comparison for Thiophanate-Methyl and Carbendazim

	Thiophanate-Methyl		Carbendazim		Combined Thiophanate-Methyl and Carbendazim
	Acute	Chronic	Acute	Chronic	Cancer
EEC[b]	**56**	**3.4**	**33**	**11**	**12.9**
Population	**DWLOC[a] (µg/L)**				
Total Population	N/A	279	N/A	314	**1**
All infants (< 1 year)	1260	80	468	90	
Children 1 - 2 years	1919	119	725	134	
Children 3 - 5 years	1933	119	732	134	
Children 6 - 12 years	2522	155	962	175	
Youth 13 - 19 years	♂ 4532	♂&♀ 280	♂ 1732	♂&♀ 315	
Adults 20 - 49 years	♂ 4540	♂&♀ 280	♂ 1738	♂&♀ 315	
Adults 50+ years	4536	279	1738	314	
Females 13 - 49 years	2067	248	299	279	

[a] DWLOC = (ARfD – food-only exposure mg/kg) × 1000 µg/mg × bw kg/water consumption L
Body weight =70, 62, 39, 15, 10 kg for adults, females, youth 6–13 years, children 1–6 years and infants, respectively.
Water consumption = 1 L/day for infants and children, 2 L/day all other populations.
[b] EEC = Drinking water estimated environmental concentration. DWLOC values larger than the corresponding EEC indicate acceptable exposure.

- The combined EEC used for the cancer assessment converted thiophanate-methyl residues to carbendazim equivalents based on the ratio of molecular weights:

$$\frac{[3.4\ \mu g\ \text{thiophanate-methyl/L}] \times [191.2\ \text{g/mol carbendazim}]}{[342.4\ \text{g/mol thiophanate-methyl}]} + [11\ \mu g/L\ \text{carbendazim}] = 12.9\ \mu g/L$$

- Shaded cell indicates DWLOC less than EEC. Potential cancer risk from drinking water exposure is uncertain, as EEC estimates are based on conservative upper bound assumptions from water modelling. Once further information on the use pattern is considered, exposure from drinking water will be reassessed.

The US Department of Agriculture had monitoring data for carbendazim in untreated and finished water from water treatment plants between the years 2004 and 2008. Carbendazim was detected infrequently, and levels were generally between 3 and 11 µg/L; however, detections in 2008 were as high as 121 µg/L.

Appendix IX Water Modelling and Monitoring for Use in Drinking Water Assessment

Modelling Results

Concentrations of thiophanate-methyl and its major transformation product carbendazim in potential drinking water sources (groundwater and surface water) were estimated in 2005 using computer simulation models. The carbendazim modelling was updated in 2009 with revised values for aerobic soil half-life and Koc. An overview of how the EECs are estimated is provided in the PMRA's Science Policy Notice SPN2004-01, *Estimating the Water Component of a Dietary Exposure Assessment*.

Estimated environmental concentrations (EECs) of thiophanate-methyl and carbendazim in groundwater were calculated using the LEACHM model, which simulates leaching through a layered soil profile over a multi-year period (20 years). The concentrations calculated using LEACHM are estimates of the flux, or movement, of pesticide into shallow groundwater with time. EECs of thiophanate-methyl and carbendazim in surface water were calculated over a multi-year period (57 - 81 years depending upon scenario) using the PRZM/EXAMS models, which simulate pesticide transport from a field into an adjacent water body and the fate of a pesticide within that water body. Pesticide concentrations in surface water were estimated in a vulnerable drinking water source, a small reservoir. The major input parameters used in the models are listed in Table 1.

Table 1 Input Parameters Used in PRZM EXAMS and LEACHM

Item	Value
Crops modelled	**apples, pears and white beans**
Maximum allowable rate per application	1.575 kg a.i./ha
Maximum number of applications per year	2
Maximum allowable rate per year	3.15 kg a.i./ha
Minimum interval between application	7 d
Timing of applications	1 April - 1 September
Solubility in water at pH 7	Thiophanate-methyl: 21.8 mg a.i./L Carbendazim: 8.0 mg a.i./L
Vapour pressure	Thiophanate-methyl: 1.3×10^{-5} mm Hg Carbendazim: 9.8×10^{-9} mm Hg
Henry's Law Constant	Thiophanate-methyl: 2.69×10^{-7} atm·m^3/mol Carbendazim: 3.1×10^{-10} atm·m^3/mol

Hydrolysis half-life	**pH 7**	Thiophanate-methyl: 36 d Carbendazim: stable
Phototransformation half-life in water		Thiophanate-methyl: 2.48 d Carbendazim: stable (32 d study)
Aerobic soil biotransformation half-life		Thiophanate-methyl: 1 d Carbendazim: 52.3 d
Aerobic aquatic biotransformation half-life		Thiophanate-methyl: 10 d Carbendazim: 61 d
Anaerobic aquatic biotransformation half-life		Thiophanate-methyl: <1 d (Modelling used 1 d) Carbendazim: 743 d
Adsorption K_{oc}		Thiophanate-methyl: 100 Carbendazim: 429

* MBC is the abbreviation used for carbendazim by USEPA

The models were run first to simulate fate and transport of the parent thiophanate-methyl. Then separate model runs were conducted for the transformation product carbendazim, assuming an application of an equivalent amount of parent compound. The application rate used in the transformation product simulation was equal to the parent application rate adjusted by the molar ratio of the transformation product to the parent, assuming 100 percent transformation. Modelled EECs for thiophanate-methyl and carbendazim are shown in Table 2.

Table 2 Estimated Exposure Concentrations Derived from the Water Models (PRZM/EXAMS and LEACHM)

Crop (annual application rate)	Compound	Groundwater (μg/L)		Reservoir (μg/L)		Dugout (μg/L)	
		Daily[1]	Yearly[2]	Daily[3]	Yearly[4]	Daily[3]	Yearly[4]
apples, pears and white beans 3.15 kg a.i./ha	Thiophanate-methyl	0	0	56 [2]	3.4 [2]	NA [5]	NA [5]
	Carbendazim *With 0.827 conversion**	4.2 *3.47*	4.2 *3.47*	3327	119.1	NA [5]	NA [5]

1 90th percentile of daily average concentrations
2 90th percentile of annual average concentrations
3 90th percentile of annual peak concentrations
4 90th percentile of annual average concentrations
5 Use in the Prairies was not considered, which eliminated the dugout
* The maximum conversion of TM to MBC of 0.827 based on results from aerobic soil metabolism study.

Water Monitoring Data

Canadian Data

A search for Canadian water monitoring data on thiophanate-methyl and carbendazim revealed that routine analysis for thiophanate-methyl and carbendazim is not conducted. The F/P/T representatives from the provinces and territories in Canada were contacted requesting water monitoring data for thiophanate-methyl and carbendazim. In addition, requests were submitted to Environment Canada, the Department of Fisheries and Oceans and the Health Canada drinking water subcommittee. No monitoring data were obtained for these two compounds.

US Data

US databases were also searched for monitoring of thiophanate-methyl and carbendazim in water. US data are also considered in the Canadian drinking water assessment given the extensive monitoring programs that exist in the US. Local use patterns, runoff events, soil and hydrogeology, as well as testing and reporting methods, are probably more important influences on residue data than northern versus southern climate. In evaluating the data, consideration is given to differences in climate, however; if temperatures are cooler, residues may degrade more slowly, whereas if temperatures are warmer, growing seasons may be longer and inputs may be more numerous and frequent.

Results of the US data search are summarized below:

- The USEPA RED[2] for thiophanate-methyl indicated that no monitoring data were known to exist for either thiophanate-methyl or carbendazim.
- The US Geological Survey National Water Quality Assessment Program (NAWQA)[3] database did not contain information on the analysis of either groundwater or surface water samples for thiophanate-methyl or carbendazim.
- The US National Contaminant Occurrence Database (NCOD)[4] did not contain any information on thiophanate-methyl or carbendazim analysis in Public Water Systems in the US.

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2 USEPA Reregistration Eligibility Decision, Thiophanate Methyl, October 2005. EPA-HQ-OPP-2004-0265-0017.

3 The National Water Quality Assessment Program (NAWQA) USGS data of residue detections from 31 integrator sites on large rivers and streams in addition to ground water sources from agricultural and urban wells. The well samples do not represent drinking water directly, and some of the wells are shallow “monitoring wells”. All samples analyzed in this program are filtered prior to analysis. http://water.usgs.gov/nawqa/

4 The National Contaminant Occurrence Database (NCOD) includes Public Water Supply (PWS) contaminant occurrence data. Water quality testing is performed at many points along public drinking water supplies, including the intake and at various points in the treatment and distribution systems, as well as at the point where the drinking water can be labeled "finished." The PWS database includes information for both groundwater and surface water sources. Positive pesticide residue detection does not *necessarily* indicate a positive detect at the end of tap - but it might - especially given the great variation in water treatment systems and their efficiency. www.epa.gov/safewater/data/ncod.html

- The US Department of Agriculture had monitoring data for carbendazim in untreated and finished water from water treatment plants between the years 2004 and 2008. Carbendazim was detected infrequently, and levels were generally between 3 and 11 µg/L; however, detections in 2008 were as high as 121 µg/L.

Drinking Water Exposure Estimates

Monitoring data and modelling estimates provide different types of information, and both are generally considered in the drinking water assessment. Pesticide concentrations in water are highly variable in time and location, and monitoring data usually do not capture the peak concentrations. Thus, monitoring data are generally considered a lower-bound estimate of the concentrations that may be expected in the environment. Modelling estimates are developed with a number of conservative assumptions and are generally considered upper-bound estimates.

No monitoring data were identified in either Canada or the US for thiophanate-methyl. The limited amount of monitoring data available for carbendazim in the US did not allow for an estimation of the residues of carbendazim in drinking water using monitoring data. The drinking water EECs for use in the dietary risk assessment of thiophanate-methyl and carbendazim are those estimated through the use of models. These estimates are considered to be reasonable upper bound values and are representative of the highest concentration of thiophanate-methyl and carbendazim that may be detected in drinking water.

Appendix X Environmental Fate, Toxicity and Potential Risk of thiophanate-methyl and the transformation product carbendazim

Table 1 Summary of the Abiotic Transformation Properties of Thiophanate-methyl and Carbendazim

Compound	Transformation Process	Half life (days)	Comments*
TPM	Hydrolysis	pH 5 stable pH 7 36 d pH 9 0.7 d	Increases with increasing pH. Main transformation product MBC and AV-195. Important route of transformation under alkaline conditions.
MBC	Hydrolysis	stable	Stable to hydrolysis at pH 5 and 7. Stability deceases with increasing pH.
TPM	Photo transformation - soil	2.9 - 5.5 d	Sandy loam pH 7. Transformation products MBC and DX-105. 10.3-19.3 d on dark controls. Important route of transformation.
MBC	Photo transformation - soil	Stable	Silt loam. 32 day study. Study duration insufficient to establish a half life.
TPM	Photo transformation - water	2.17 d (0.53 d - 2.48 d)	pH 5. Natural sunlight. Transformation products MBC and DX-105. Important route of transformation.
MBC	Photo transformation - water	Stable	pH 5.

TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA
* All data from USEPA RED (2004).

Table 2 Summary of Biotransformation Properties of Thiophanate-methyl and Carbendazim

Compound	Transformation Process	Half life (days)	Interpretation	Major Transformation Products
TPM	Aerobic soil biotransformation	<1 (3 soils: pH 5 to 7.5)	Nonpersistent	MBC
MBC	Aerobic soil biotransformation	52.3 (7 soils: pH 4.7 to 6.8)	Moderately persistent	none
TPM	Aerobic water-sediment biotransformation	No data.	--	--
MBC	Aerobic water-sediment biotransformation	61 (1 soil pH 7.3)	Moderately persistent	none
TPM	Anaerobic water-sediment biotransformation	<1 (1 soil pH 6.2)	Nonpersistent	MBC

TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA

Table 3 Summary of Thiophanate-methyl and Carbendazim Mobility

Soil Type	pH	om %	USEPA RED Reported Values			PMRA Calculated Values	
			K_{oc} (L/kg)	K_f (L/kg)	1/n	K_d*	K_{oc}
Studies: Thiophanate-methyl							
Soil 1: loamy sand	6.5	2.1	118	1.46	0.774	0.87	71.2
Soil 2: loam	6.4	1.2	137	0.97	0.827	0.65	93.6
Soil 3: sandy loam	7.1	0.6	189	0.66	0.903	0.53	152
Soil 4: sand	8	0.2	225	0.27	0.894	0.21	182
Soil 5: loam	6.9	0.7	359	1.47	0.789	0.9	223
Soil 6: clay loam	5.2	2.9	859	14.1	0.754	8	476

Soil Type	pH	om %	USEPA RED Reported Values			PMRA Calculated Values	
			K_{oc} (L/kg)	K_f (L/kg)	1/n	K_d*	K_{oc}
Studies: Carbendazim							
EPA Model			1885				
Soil 1: sandy loam	7.1	0.6	-	3.77	0.77	3.2	915
Soil 2: loam	6.4	1.2	-	4.74	0.712	4.37	616
Soil 3: sand	8	0.2	-	0.45	0.827	0.34	282
Soil 4: clay loam	5.2	2.9	-	88.2	0.609	451	27306
Soil 5: loam	6.9	0.7	-	4.47	0.752	3.83	934
Soil 6: loamy sand	6.5	2.1	-	5.71	0.747	5.32	429

Table 4 Summary of Terrestrial Field Dissipation of Thiophanate-methyl and Carbendazim

Compound	Type of the study	Half life* (days)	Comments
TPM	Field dissipation soil	1 d	Loamy sand. No TPM detected after 12 months. Transformation products MBC and allophanate. Not persistent.
TPM	Field dissipation soil	4.2 d	Sandy loam. No TPM detected after 14 days. Transformation products MBC. Not persistent.
MBC	Field dissipation soil	94 d	Loamy sand. Moderately persistent. No MBC detected after 12 months.
MBC	Field dissipation soil	33.9 d	No MBC detected after 120 days. Slightly persistent.
MBC	Field dissipation soil	15 d	Sandy soil, Florida. Transformation product 2-AB(2-aminobenzimidazole).
MBC	Field dissipation soil	86 d	Loam. California. Transformation product 2-AB(2-aminobenzimidazole).
TPM	Field dissipation apple orchard	<1 d	Dissipated too rapidly for half life to be determined.

Compound	Type of the study	Half life* (days)	Comments
MBC	Field dissipation apple orchard	22 d	Slightly persistent.
TPM	Field dissipation foliage apple orchard	3.8 d	New York. MBC levels not reported. Nonpersistent.
TPM	Field dissipation foliage apple orchard	31.4 d	Washington State. MBC levels not reported. Slightly persistent.

*Referred to as half life in USEPA RED (2004)
TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA

Table 5 Environmental toxicity of thiophanate-methyl and carbendazim to terrestrial organisms

Organism	Study type	Species		Endpoint	Value (effect)	Comments	Reference
Terrestrial Species							
Invertebrate	Acute	Honey bee (*Apis mellifera*)		48-h LD50 (contact)	>100 µg a.i./bee	Relatively nontoxic.	USEPA RED, 2004
		Earthworm (*Eisenia foetida*)	TPM	NOEC	0.60 kg a.i./ha	--	PMRA #s 1530416 1530417
			MBC	LOEC	0.15 kg a.i./ha	--	
Birds	14-day acute oral	Bobwhite quail (*Colinus virginianus*)		LD50	>4,640 mg a.i./kg bw	Practically nontoxic.	USEPA RED, 2004
		Mallard Duck (*Anas platyrhynchos*)		LD50	4640 mg a.i./kg bw	Practically nontoxic.	USEPA RED, 2004
	5-day dietary	Bobwhite quail (*Colinus virginianus*)		LC50	>10,000 mg aikg diet	Practically nontoxic.	USEPA RED, 2004
		Mallard Duck (*Anas platyrhynchos*)		LC50	>10,000 mg aikg diet	Practically nontoxic.	USEPA RED, 2004
	Reproduction	Bobwhite quail (*Colinus virginianus*)		NOEC	>150 & >500 mg aikg diet	--	USEPA RED, 2004
		Mallard Duck (*Anas platyrhynchos*)		NOEC	>103 mg aikg diet	Effects on eggs and body weight	USEPA RED, 2004

Organism	Study type	Species	Endpoint	Value (effect)	Comments	Reference
Mammals	Acute oral	Rat (*Rattus norvegicus*)	LD50	>5,000 mg a.i./kg bw	Practically nontoxic.	USEPA RED, 2004
	Reproduction	Rat (*Rattus norvegicus*)	NOEC	195 (or 130?) mg /kg bw/day	--	USEPA RED, 2004
			NOEC	1300 mg /kg diet	Converted value	USEPA RED, 2004

TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA

Table 6 Environmental toxicity of thiophanate-methyl and carbendazim to aquatic organisms

Organism	Study type	Species	Endpoint		Value (effect)	Comments	Reference
Freshwater Organisms							
Invertebrate	Acute	*Daphnia magna*	TPM	48-h LC50	5.4 mg a.i./L	Moderately toxic	USEPA RED, 2004
			MBC	48-h LC50	5.4 mg a.i./L	Moderately toxic	USEPA RED, *Daphnia magna* 2004
	Chronic (life-cycle)	*Daphnia magna*	MBC	21-d NOEC	0.003 mg a.i./L		USEPA RED, 2004
		Daphnia magna	MBC	21-d NOEC	0.0177 mg a.i./L		PMRA # 1530460
Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	TPM	96-h LC50	8.3 mg a.i./L	Moderately toxic	USEPA RED, 2004
		Bluegill sunfish (*Lepomis macrochirus*)	TPM	96-h LC50	>41 mg a.i./L	Slightly toxic	USEPA RED, 2004
	Early Life Cycle	Rainbow trout (*Oncorhynchus mykiss*)	TPM	28-d NOEC	0.32 mg a.i./L		PMRA # 1530423
	Early Life Cycle	Channel Catfish (*Ictalurus punctatus*)	MBC	9-d NOEC	1.01-1.52 mg a.i./L		USEPA RED, 2004

Organism	Study type	Species	Endpoint		Value (effect)	Comments	Reference
Vascular aquatic plants		Duckweed (*Lemna gibba*)	TPM	EC50	>2.4 mg a.i./L		
			TPM	NOEC	2.4 mg a.i./L		
Algae		Green algae (*Selenastrum capricornutum)*	TPM	EC_{50}	>0.95 mg a.i./L		
		Green algae (*Selenastrum capricornutum)*	TPM	NOEC	0.95 mg a.i./L		
		Blue-green algae (*Anabaena flos-aquae*)	TPM	EC_{50}	>4.3 mg a.i./L		
		Blue-green algae (*Anabaena flos-aquae*)	TPM	NOEC	4.3 mg a.i./L		
		Freshwater diatom (*Navicula pelliculosa*)	TPM	EC_{50}	0.93 mg a.i./L		
		Freshwater diatom (*Navicula pelliculosa*)	TPM	NOEC	0.43 mg a.i./L		
	Acute	Marine diatom (*Skeletonema costatum*)	TPM	EC50	1.7 mg a.i./L		
		Marine diatom (*Skeletonema costatum*)	TPM	NOEC	0.11 mg a.i./L		
Estuarine/marine fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	TPM	96 h LC50	40		
				acute NOEC	17		
Estuarine/marine invertebrates	Acute	Eastern Oyster (*Crassostrea virginica*)	TPM	NOEC	2.2 mg a.i./L		
	Acute	Mysid Shrimp (*Americamysis bahia*)	TPM	96 hr LC50	1.1 mg a.i./L		
	Chronic (life-cycle)	Mysid Shrimp (*Americamysis bahia)*	TPM	96 hr LC50	0.025 mg a.i./L		

TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA

Table 7 Summary of Screening Level Risk Assessment of Thiophanate-methyl and Carbendazim to Terrestrial Organisms (Invertebrates)

Organism	Exposure	Endpoint		Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[1]
Invertebrates					
Earthworm	Chronic	TPM	NOEC 0.60 kg a.i./ha	0.395	0.7
				12.25	**20.4**
		MBC	LOEC 0.15 kg a.i./ha	0.359	**2.4**
				5.65	**37.7**
Honeybee	Acute	TPM	11.2 kg a.i./ha	0.728	0.07
				12.25	**1.56**

[1] Bold fonts indicates exceedance of LOC
TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA

Table 8 Summary of Screening Level Risk Assessment of Thiophanate-methyl to Terrestrial Organisms (Birds and Mammals)

Organism	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[1]
Birds				
Mallard	Acute oral	NOEL 464 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.002
			12.25	0.04
	Acute dietary	1000 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.03
			12.25	0.41
	Reproduction	NOEC 103 mg a.i./kg diet	0.728	0.24
			12.25	**4.02**
Bobwhite quail	Acute oral	NOEL 464 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.03
			12.25	0.42
	Acute dietary	1000 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.127
			12.25	**2.145**

Organism	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[1]
American Robin	Acute oral	308 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.08
			12.25	**1.43**
	Acute dietary	345 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.083
			12.25	**1.4**
Field Sparrow	Acute oral	238 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.12
			12.25	**2.5**
	Acute dietary	703 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.12
			12.25	**2**
Mammals				
Rat	Acute oral	NOEL 500 mg ae/kg bw (0.1 × LD_{50})	0.728	0.01
			12.25	**2.13**
	Acute dietary	291.7 Estimated NOEC mg ae/kg diet (0.1x LC_{50})	0.728	**1.26**
			12.25	**21.2**
Mouse	Reproduction	NOEC 1300 mg a.i./kg diet	0.728	0.281
			12.25	**4.73**

[1] Bold fonts indicate exceedance of the LOC

Table 9 Summary of Refined[1] Level Risk Assessment of Thiophanate-methyl and Carbendazim to Terrestrial Organisms (Invertebrates)

Organism	Exposure	Endpoint		Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[2]
Invertebrates					
Earthworm	Chronic	TPM	NOEC 0.60 kg a.i./ha	0.395	0.08
				12.25	**1.35**
		MBC	LOEC 0.15 kg a.i./ha	0.359	0.26
				5.65	**4.14**
Honeybee	Acute	TPM	11.2 kg a.i./ha	0.728	0.01
				12.25	0.17

[1] Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
[2] Bold fonts indicates exceedance of LOC
TPM: thiophanate-methyl
MBC: the abbreviation used for carbendazim by USEPA

Table 10 Summary of Refined[1] Level Risk Assessment of Thiophanate-methyl to Terrestrial Organisms (Birds and Mammals)

Organism	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[2]
Birds				
Mallard	Acute oral	NOEL 464 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.0002
			12.25	0.004
	Acute dietary	1000 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.003
			12.25	0.05
	Reproduction	NOEC 103 mg a.i./kg diet	0.728	0.03
			12.25	0.44
Bobwhite quail	Acute oral	NOEL 464 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.003
			12.25	0.05
	Acute dietary	1000 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.01
			12.25	0.24
American Robin	Acute oral	308 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.009
			12.25	0.16
	Acute dietary	345 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.01
			12.25	0.15
Field Sparrow	Acute oral	238 mg a.i./kg bw (1/10 of LD_{50})	0.728	0.013
			12.25	0.28
	Acute dietary	703 mg a.i./kg diet (1/10 of LC_{50})	0.728	0.01
			12.25	0.22
Mammals				
Rat	Acute oral	NOEL 500 mg ae/kg bw (0.1 × LD_{50})	0.728	0.001
			12.25	0.23
	Acute dietary	291.7 Estimated NOEC mg ae/kg diet (0.1x LC_{50})	0.728	0.14
			12.25	**2.3**
Mouse	Reproduction	NOEC 1300 mg a.i./kg diet	0.728	0.03
			12.25	0.52

1 Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
2 Bold fonts indicates exceedance of LOC

Table 11 Summary of Screening Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Freshwater Aquatic Invertebrates (*Daphnia magna*)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[2]
Thiophanate-methyl	Acute	2.7 mg a.i./L (0.5 × LC_{50})	0.395	0.018
			12.25	0.567
Carbendazim	Acute	2.7 mg a.i./L (0.5 × LC_{50})	0.2773	0.01
			4.5123	0.209
Carbendazim	Chronic (life cycle)	0.003 mg a.i./L (21 d NOEC)	0.277	**9.3**
			4.512	**188**

1 Half life of thiophanate-methyl in water = 1 d; Half life of carbendazim in water = 61 d
2 Bold fonts indicates exceedance of LOC
3 Equivalent cumulative application rates

Table 12 Summary of Refined[1] Level Assessment of Risk of Carbendazim to Aquatic Invertebrates (*Daphnia magna*)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[2]
Carbendazim	Chronic (life cycle)	0.003 mg a.i./L (21 d NOEC)	0.277	**1**
			4.512	**20.7**

1 Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
2 Bold fonts indicates exceedance of LOC

Table 13 Summary of Refined Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Aquatic Invertebrates (*Daphnia magna*) based on exposure to runoff[2]

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	EEC mg a.i./L	RQ[1]
Thiophanate-methyl	Acute	2.7 mg a.i./L ($0.5 \times LC_{50}$)	0.395	5.64×10^{-3}	0.002
			12.25	80.5×10^{-3}	0.03
Carbendazim	Acute	2.7 mg a.i./L ($0.5 \times LC_{50}$)	0.277	15.4×10^{-3}	0.006
			4.512	86.8×10^{-3}	0.032
Carbendazim	Chronic (life cycle)	0.003 mg a.i./L (21 d NOEC)	0.277	14.1×10^{-3}	**4.7**
			4.512	70.7×10^{-3}	**23.6**

1 Bold fonts indicates exceedance of LOC
2 Runoff EECs:
Thiophanate-methyl: 90% centile peak water EEC
Carbendazim: Acute: 90% centile peak water EEC
Carbendazim: Chronic: 90% centile 21 day water EEC

Table 14 Summary of Screening Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Estuarine/Marine Aquatic Invertebrates (Mysid Shrimp)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[1]
Thiophanate-methyl	Acute	0.55 mg a.i./L ($0.5 \times LC_{50}$)	0.395	0.089
			12.25	**2.784**
Carbendazim	Chronic (life cycle)	0.025 mg a.i./L (NOEC)	0.277	**1.12**
			4.512	**22.56**

1 Bold fonts indicates exceedance of LOC

Table 15 Summary of Refined[1] Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Estuarine/Marine Aquatic Invertebrates (Mysid Shrimp)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[2]
Thiophanate-methyl	Acute	0.55 mg a.i./L (0.5 × LC_{50})	12.25	0.31
Carbendazim	Chronic (life cycle)	0.025 mg a.i./L (NOEC)	0.277	0.12
			4.512	**2.48**

1 Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
2 Bold fonts indicates exceedance of LOC

Table 16 Summary of Refined Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Estuarine/Marine Aquatic Invertebrates (Mysid Shrimp) based on exposure to runoff [2]

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	EEC mg a.i./L	RQ[1]
Thiophanate-methyl	Acute	0.55 mg a.i./L (0.5 × LC_{50})	0.395	5.34×10^{-3}	0.1
			12.25	76.3×10^{-3}	**1.4**
Carbendazim	Chronic (life cycle)	0.025 mg a.i./L (NOEC)	0.277	14.1×10^{-3}	0.56
			4.512	70.7×10^{-3}	**2.83**

1 Bold fonts indicates exceedance of LOC
2 Runoff EECs:
Thiophanate-methyl: 90% centile 96 hr water EEC
Carbendazim: 90% centile 21 day water EEC

Table 17 Summary of Screening Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Freshwater Fish (Rainbow Trout and Channel Catfish)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[1]
Thiophanate-methyl	Acute	0.83 mg a.i./L ($0.1LC_{50}$) Rainbow trout	0.395	0.059
			12.25	**1.845**
Carbendazim	Chronic (Early life cycle)	1.01 mg a.i./L NOEC Channel Catfish	0.277	0.028
			4.512	0.558

Table 18 Summary of Refined[1] Level Assessment of Risk of Thiophanate-methyl to Freshwater Fish (Rainbow Trout)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[2]
Thiophanate-methyl	Acute	0.83 mg a.i./L ($0.1LC_{50}$)	12.25	0.2

1 Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
2 Bold fonts indicates exceedance of LOC

Table 19 Summary of Refined Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Freshwater Fish (Rainbow Trout and Channel Catfish) based on exposure to runoff[2]

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	EEC mg a.i./L	RQ[1]
Thiophanate-methyl	Acute	0.83 mg a.i./L ($0.1LC_{50}$) Rainbow trout	0.395	5.64×10^{-3}	0.068
			12.25	80.5×10^{-3}	0.97
Carbendazim	Chronic (Early life cycle)	1.01 mg a.i./L NOEC Channel Catfish	0.277	5.97×10^{-3}	0.01
			4.512	14.5×10^{-3}	0.014

1 Bold fonts indicates exceedance of LOC
2 Runoff EECs:
Thiophanate-methyl:: 90% centile Peak Water EEC
Carbendazim: Ave. 90% centile Annual Water EEC

Table 20 Summary of Screening Level Assessment of Risk of Thiophanate-methyl to Estuarine/Marine Fish (Sheepshead Minnow)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[1]
Thiophanate-methyl	Acute	17 mg a.i./L NOEC	0.395	0.003
			12.25	0.09

1 Bold fonts indicates exceedance of LOC

Table 21 Summary of Screening Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Amphibians (Rainbow Trout and Channel Catfish Surrogate Data)

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)[1]	RQ[1]
Thiophanate-methyl	Acute	0.83 mg a.i./L ($0.1LC_{50}$)	0.395	0.317
			12.25	**9.8**
Carbendazim	Chronic (Early life cycle)	1.01 mg a.i./L NOEC	0.277	0.149
			4.512	**3.04**

1 Bold fonts indicates exceedance of LOC

Table 22 Summary of Refined[1] Level Assessment of Risk of Thiophanate-methyl to Amphibians (Rainbow Trout and Channel Catfish Surrogate Data)

Compound	Exposure	Endpoint	Cumulative Max. Use Rate (kg a.i./ha)[1]	RQ[2]
Thiophanate-methyl	Acute	0.83 mg a.i./L ($0.1LC_{50}$) Rainbow trout	12.25	1.08
Carbendazim	Early Life Stage	1.01 mg a.i./L NOEC Channel Catfish	4.512	0.33

1 Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
2 Bold fonts indicates exceedance of LOC

Table 23 Summary of Refined Level Assessment of Risk of Thiophanate-methyl and Carbendazim to Amphibians (Rainbow Trout and Channel Catfish Surrogate Data) based on exposure to runoff[2]

Compound	Exposure	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	EEC mg a.i./L	RQ[1]
Thiophanate-methyl	Acute	0.83 mg a.i./L ($0.1LC_{50}$) Rainbow trout	0.395	5.64×10^{-3}	0.068
			12.25	80.5×10^{-3}	0.97
Carbendazim	Chronic (Early life cycle)	1.01 mg a.i./L NOEC Channel Catfish	0.277	5.97×10^{-3}	0.01
			4.512	14.5×10^{-3}	0.014

1 Bold fonts indicates exceedance of LOC
2 Runoff EECs:
Thiophanate-methyl:: 90% centile Peak Water EEC
Carbendazim: Ave. 90% centile Annual Water EEC

Table 24 Summary of Screening Level Assessment of Risk from Thiophanate-methyl/Carbendazim to Freshwater Aquatic Plants and Algae and Freshwater and Marine Diatoms

Species	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[1]
Lemna gibba (freshwate plant)	2.4 mg a.i./L (0.5×14 day $EC_{50)}$)	0.395	0.02
		12.25	0.638
Kirchneria subcapitata (freshwater alga)	0.48 mg a.i./L (0.5×5 day EC_{50})	0.395	0.102
		12.25	**3.19**
Navicula pelliculosa (freshwater diatom)	0.47 mg a.i./L (0.5×5 day EC_{50})	0.395	0.104
		12.25	**3.26**
Skeletonema costatum (marine diatom)	0.85 mg a.i./L (0.5×5 day EC_{50})	0.395	0.06
		12.25	**1.8**

[1] Bold fonts indicates exceedance of LOC

Table 25 Summary of Refined[1] Level Assessment of Risk from Thiophanate-methyl/Carbendazim to Freshwater Aquatic Plants and Algae and Freshwater and Marine Diatoms

Species	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	RQ[2]
Kirchneria subcapitata (freshwater alga)	0.48 mg a.i./L (0.5×5 day EC_{50})	12.25	0.35
Navicula pelliculosa (freshwater diatom)	0.47 mg a.i./L (0.5×5 day EC_{50})	12.25	0.35
Skeletonema costatum (marine diatom)	0.85 mg a.i./L (0.5×5 day EC_{50})	12.25	0.2

[1] Refined risk based on exposure to drift of 11% of the application rate, for a default droplet size of fine (fungicides)
[2] Bold fonts indicates exceedance of LOC

Table 26 Summary of Refined Level Assessment of Risk from Thiophanate-methyl/Carbendazim to Freshwater Aquatic Plants and Algae and Freshwater and Marine Diatoms based on exposure from runoff[2]

Species	Endpoint	Cumulative Min. and Max. Use Rate (kg a.i./ha)	EEC mg a.i./L	RQ[1]
Lemna gibba (freshwate plant)	2.4 mg a.i./L (0.5 × 14 day EC_{50})	0.395	5.34×10^{-3}	0.002
		12.25	76.3×10^{-3}	0.032
Kirchneria subcapitata (freshwater alga)	0.48 mg a.i./L (0.5 × 5 day EC_{50})	0.395	5.34×10^{-3}	0.011
		12.25	76.3×10^{-3}	0.159
Navicula pelliculosa (freshwater diatom)	0.47 mg a.i./L (0.5 × 5 day EC_{50})	0.395	5.34×10^{-3}	0.011
		12.25	76.3×10^{-3}	0.16
Skeletonema costatum (marine diatom)	0.85 mg a.i./L (0.5 × 5 day EC_{50})	0.395	5.34×10^{-3}	0.006
		12.25	76.3×10^{-3}	0.09

[1] Bold fonts indicates exceedance of LOC
[2] Runoff EECs:
Thiophanate-methyl/Carbendazim : 90% centile 96 hr water EEC

Appendix XI Alternative registered active ingredients to thiophanate-methyl for site-pest combinations of Commercial Class products (registered alternatives according to the PMRA ELSE database as of April 7, 2006). Revised October 22, 2008 based on comments from the public on REV 2007-12 and to reflect changes in the re-evaluation and registration status of the alternatives identified in 2006

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (Resistance Management Group No.)[2,3]	Non-chemical Control Methods[1]	Registrant Supports Use of thiophanate-methyl (Y/N/M[4])
Apple	Apple scab	Minor (BC and Western provinces) to prevalent (Eastern provinces)	Group 3: Flusilazole Group 9: Cyprodinil Group 11: Kresoxim-methyl, trifloxystrobin, Group U: Dinocap [7] Group M: Lime sulphur or calcium polysulphide [6], mancozeb [6], metiram [6], captan [6], Dodine [7]	Resistant varieties (i.e. Liberty, Goldrush). Water management (shut off sprinklers to reduce leaf wetness). Orchard design and pruning to improve aeration and penetration. Reducing primary inoculum (i.e. removal or decomposition of leaf litter).	Y
	Powdery mildew	Rare to minor in (BC, PE, NS, NB, QC and ON)	Group 3: Flusilazole, Myclobutanil [6], Triforine [6] (non-bearing trees only) Group 9: Cyprodinil Group 11: Kresoxim-methyl, Trifloxystrobin, Group U: Dinocap [7] Group M: Lime sulphur or calcium polysulphide [6], Sulphur [7], Mancozeb [6]	Avoiding overcrowding of trees and branches. Pruning out twigs with white fungus growth on the surface.	Y
Pear	Pear scab	Rare except in Ontario where it is prevalent	Group 11: Kresoxim-methyl Group M: Lime sulphur or calcium polysulphide [6], Ferbam [6], Captan [6], Dodine [7]	Reducing primary inoculum (i.e. removal or decomposition of leaf litter).	Y
	Powdery mildew	Rare	Group 11: Kresoxim-methyl, Trifloxystrobin, Group M: Lime sulphur or calcium polysulphide [6], Sulphur [7]	Avoid planting Anjou pears near susceptible apple cultivars. Bartlett and Flemish Beauty are more resistant to powdery mildew.	Y
Lowbush blueberries	Blossom blight and twig blight (*Botrytis* sp.)	Minor / once every five years	Group 7: Boscalid Group 11: Pyraclostrobin Group 17: Fenhexamid Group M: Ferbam [6]	Burn-pruning every second or third crop cycle to reduce overwintering inoculum. Control weeds within and surrounding the field.	Y, M
Raspberries	Fruit rot	Minor except in BC, ON and QC where it is prevalent/ every year	Group 2: Iprodione Group 7: Boscalid Group 17: Fenhexamid Group M: Captan [6]	Train canes to promote good air circulation. Avoid excessive nitrogen fertilization. Time overhead irrigation so that plants dry quickly. Cool harvested fruits quickly.	Y
	Powdery mildew	Minor/ more prevalent in dry years	None	Train canes to promote good air circulation. Use good row spacing. Remove diseased material and destroy in the fall .	Y

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (Resistance Management Group No.) [2,3]	Non-chemical Control Methods[1]	Registrant Supports Use of thiophanate-methyl (Y/N/M[4])
Strawberry	Fruit rot (*Botrytis* sp.)	Minor except in ON, QC, NB, NS, and PE where it is prevalent/ every year	Group 2: Iprodione [6], Vinclozolin [7] Group 7: Boscalid Group 17: Fenhexamid Group M: Captan [6], Folpet [6], Lime sulphur or calcium polysulphide [6] Thiram [6]	Weed control to reduce long periods of leaf wetness. Avoid excessive nitrogen fertilization. Irrigate during the day and for short periods. Use narrow rows to reduce plant density. Incorporate plant residues.	Y
	Leaf Spot	Minor to moderate in ON and QC/ every year	Group 17: Fenhexamid Group M: Captan [6], Dodine [7], Folpet [6], Copper as elemental, present as tribasic copper sulphate [6]	Plant resistant or less susceptible cultivars (e.g. Chambly, Vantage).Use certified plants for new plantings.	Y
Peach	Brown rot	Moderate to prevalent in BC and ON, minor elsewhere/ every year	Group 2: Iprodione [6] Group 3: Fenbuconazole, Myclobutanil, Propiconazole [6], Triforine [6] Group 7: Boscalid Group 9: Cyprodinil Group 17: Fenhexamid Group M: Captan [6], Ferbam [6], Chlorothalonil [6], Sulphur [7], Thiram [6]	Prune out twigs killed by the fungus. Dispose of mummified fruits on the trees and soil surface. Avoid fruit bruising and punctures.	Y
Nectarine	Brown rot	Moderate to prevalent in BC and ON, minor elsewhere /every year	Group 3: Fenbuconazole, Myclobutanil , Propiconazole [6] Group 7: Boscalid Group 9: Cyprodinil Group 17: Fenhexamid Group M: Captan [6], Chlorothalonil [6]	Prune out twigs killed by the fungus. Dispose of mummified fruits on the trees and soil surface. Avoid fruit bruising and punctures.	Y
Plums	Brown rot	Moderate to prevalent in BC and ON, minor elsewhere/ every year	Group 2: Iprodione [6] Group 3: Fenbuconazole, Propiconazole [6], Triforine [6] Group 7: Boscalid Group 9: Cyprodinil Group M: Captan [6], Ferbam [6], Sulphur [7]	Prune out twigs killed by the fungus. Dispose of mummified fruits on the trees and soil surface. Avoid fruit bruising and punctures.	Y
Prunes	Brown rot	Moderate to prevalent in BC and ON, minor elsewhere/ every year	Group 2: Iprodione [6] Group 3: Fenbuconazole, Triforine [6] Group 7: Boscalid Group 9: Cyprodinil Group M: Captan [6], Ferbam [6], Sulphur [7]	Prune out twigs killed by the fungus. Dispose of mummified fruits on the trees and soil surface. Avoid fruit bruising and punctures.	Y
Cherries (sour and sweet)	Brown rot	Moderate to prevalent in BC and ON, minor elsewhere/ every year	Group 2: Iprodione [6] Group 3: Fenbuconazole, Myclobutanil , Propiconazole [6], Triforine [6] Group 7: Boscalid Group 17: Fenhexamid Group M: Captan,[6] Chlorothalonil [6], Ferbam [6], Sulphur [7], Copper as elemental, present as tribasic copper sulphate [6] (sour cherries only) or as copper oxychloride [6] (sour cherries only)	Prune out twigs killed by the fungus. Dispose of mummified fruits on the trees and soil surface. Avoid fruit bruising and punctures.	Y
White beans	White mould	Major / every year	Group 2: Iprodione [6], Vinclozolin [7] Group 7: Boscalid Group 14: Dichloran [6] Group M: Captan [6]	Resistant cultivars (e.g. Rico 23). Rotation of 4 years. Plant spacing to allow air circulation. Avoid excess fertilization.	Y

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (Resistance Management Group No.)[2,3]	Non-chemical Control Methods[1]	Registrant Supports Use of thiophanate-methyl (Y/N/M[4])
Turf	Brown patch	Minor /every year in ON and QC; minor/ 1 in 5 years elsewhere	Group 2: Iprodione [6] Group 3: Myclobutanil , Propiconazole [6] Group 11: Azoxystrobin, Trifloxystrobin Group 14: Quintozene [6] Group M: Captan [6], Chlorothalonil [6]	Balanced fertility. Adequate irrigation (i.e. avoid night watering). Cultivate to alleviate compaction. Thatch management and proper mowing height. Species adapted for the intended use and selection of resistant cultivars if available.	Y
	Dollar spot	Major / every year	Group 2: Iprodione [6] Group 3: Myclobutanil , Propiconazole [6] Group 7: Boscalid Group M: Anilazine [7], Chlorothalonil [6], Thiram [6]	Limit the amount and duration of leaf wetness, reduce shade, mow the turf in early morning to displace dew, avoid watering at night. Use adequate nitrogen fertilization. Use resistant cultivars.	Y
	Copper spot	Minor	Group M: Anilazine [7]	Velvet bentgrass is most susceptible. Use other turf species or resistant cultivars.	Y
	Pink snow mould	Major/ every year	Group 2: Iprodione[6] Group 3: Propiconazole[6] Group 7: Carbathiin [6], Oxycarboxin [6] Group 11: Azoxystrobin, Trifloxystrobin Group 14: Quintozene [6], Chloroneb [6] Group M: Chlorothalonil[6], Thiram [6]	Balanced fertility. Snow removal/ snow cover. Adequate irrigation. Cultivation to alleviate compaction. Thatch management and proper mowing height. Species adapted for the intended use and selection of resistant cultivars if available.	Y
Rose and ornamental plants (outdoors)	Black spot	Minor/ every year	Group 3: Myclobutanil, Triforine [6] Group M: Captan [6], Chlorothalonil [6], Copper as elemental, present as tribasic copper sulphate [6]	Prune and discard infected branches or leaves. Allow good air circulation. Use resistant cultivars.	Y
	Powdery mildew	Major/ every year	Group 3: Myclobutanil, Triforine [6] Group 5: Dodemorph-acetate [6] Group M: Copper as elemental, present as tribasic copper sulphate [6], Folpet [6] Non-conventional, biopesticide: QST strain of *Bacillus subtilis* (suppression, roses and a few other ornamentals)	Use resistant cultivars. Prune and discard infected branches or leaves before new growth starts in the spring. Allow good air circulation.	Y
Aspen and Poplar	Marssonnina and septoria leaf spots	Minor/ every year	Group M: Chlorothalonil [6] (Marssonnina only, none registered for septoria leaf spot control)	Remove or bury diseased leaves. Use only cuttings from disease-free material. Use resistant clones in hybrid poplar plantations.	Y

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (Resistance Management Group No.)[2,3]	Non-chemical Control Methods[1]	Registrant Supports Use of thiophanate-methyl (Y/N/M[4])
Greenhouse potted ornamentals	Powdery mildew	Moderate / every year	Group 3: Myclobutanil (Roses, Gerbera, Aster and Chrysanthemums) Group 5: Dodemorph-acetate [6] (greenhouse roses) Group M: Chlorothalonil [6]	Keep doors closed. Maintain smooth airflow. Use humidity control program. Use radiant heat to maintain a dry environment, reduce heat loss at night.	Y
	Botrytis sp.	Moderate/ every year	Group 14: Dichloran [6] (Rose, Geranium and Chrysanthemum) Group 17: Fenhexamid Group M: Chlorothalonil [6]	Keep foliage and flowers dry. Avoid overhead watering. Provide good air circulation. Remove infected plant material. Use disease free propagating material.	Y
	Fusarium stem, crown and root rots	Minor/ every year	Group M: Captan [6] Non-conventional, biopesticide: *Streptomyces griseoviridis* strain K61(suppression) *Trichoderma harzianum* Rifai strain KRL-AG2 (suppression)	Avoid hot or cold temperature extremes. Irrigate consistently, avoid too wet or too dry extremes. Use appropriate media. Pasteurise soil if used. Use disease-free stock for propagation.	Y
	Rhizoctonia stem, crown and root rots	Minor/ every year	Group 2: Iprodione Group 11:Trifloxystrobin Group 14: Quintozene [6]	Use appropriate media. Pasteurise soil if used. Use disease-free stock for propagation.	Y
	Leaf spots	Minor/ every year	Group M: Chlorothalonil [6], Captan [6] (carnation leaf spot only)	Keep foliage and flowers dry. Avoid overhead watering. Provide good air circulation. Use disease free propagating material.	Y
Potato (seed treatment cut seed)	Black leg	Minor/ every year	Group 12: Fludioxonil Group M: Captan [6]	Use disease-free seed. Warm seed tubers for 4 to 10 days before cutting. Plant cut seed immediately. Disinfect appropriately. Practice good sanitation procedures. Plant seed in warm soil (greater than 10ºC).	Y
Potato (seed treatment cut seed)	Fusarium rot	Moderate/ every year	Group 12: Fludioxonil Group M: Mancozeb [6], Metiram [6]	Plant clean, disease-free seed. Plant cut seed immediately, or store under adequate ventilation, high humidity, and to a temperature of 15ºC prior to planting. Clean farm equipment. Harvest during dry, cool weather.	Y
	Seed piece decay	Moderate/ every year	Group M: Captan [6], Mancozeb [6], Metiram [6]	Avoid planting under unfavourable weather conditions.	Y
	Silver scurf	Major/ every year	Group 12: Fludioxonil	Plant certified silver scurf-free seed. Avoid planting in fields that had disease the previous season. Thoroughly disinfect storage areas. Harvest as soon as possible. Reduce the amount of soil and plant debris going into the storage. Use air to dry wet tubers. Remove field heat from tubers as soon as possible, and avoid condensation in storage.	Y, M

Site(s)	Pest	Pest Status / Incidence[1]	Alternative Registered Active Ingredients (Resistance Management Group No.) [2,3]	Non-chemical Control Methods[1]	Registrant Supports Use of thiophanate-methyl (Y/N/M[4])
Potato (seed treatment cut seed)	Verticillium wilt	Rare to minor in ON, QC, NB, NS and PE/ every year	Group M: Captan [6] (aid in the control of verticillium wilt)	Maintain optimum fertility. Do not over-water. Green manure incorporation may reduce disease severity. Practice a three to four year rotation. Avoid contamination with soil from diseased fields, diseased tubers or plant refuse.	Y
Dry common beans (seed treatment)	Seed borne anthracnose	Major in ON and MB/every year	Group 7: Carbathiin [6] + Group M : Thiram [6] Group 12: Fludioxonil + Group 4: Metalaxyl-m (mefenoxam)[7]	Follow a three year rotation. Use disease free seed. Bury crop debris. Avoid entering fields during wet weather. Plant resistant cultivars to the delta race (e.g. OAC Seaforth).	Y
Sweet corn (seed treatment)	*Penicillium oxalicum, Penicillium spp.*	Rare to sporadic in ON and QC	Group 12: Fludioxonil Group 3: Difenoconazole +Group 4: Metalaxyl-m (mefenoxam)[7]		Y, M

[1] Data from Agriculture and Agri-Food Canada Crop Profiles, end user surveys and research by the PMRA.

[2] This is a list of registered options only. Health Canada does not endorse any of the options listed. A number of the listed alternative active ingredients are in the process of being re-evaluated by Health Canada, including the following active ingredients for which information update documents have been published: Metalaxyl-m (mefenoxam), sulphur and vinclozolin. The registration status of active ingredients under re-evaluation may change pending the final regulatory decision. For additional information, consult the PMRA publications website: www.hc-sc.gc.ca/cps-spc/pubs/pest/index-eng.php or www.hc-sc.gc.ca/cps-spc/pubs/pest/index-fra.php .

[3] Fungicide Resistance Management Group Numbers (DIR 99-06, *Voluntary pesticide resistance management labelling initiative based on target site/mode of action*):
2 = affect cell division, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) synthesis and metabolism; 3 = demethylation inhibitor (DMI): inhibition of demethylation in sterol biosynthesis; 4 = phenylamides (affect RNA synthesis); 5 = morpholines (inhibition of an isomerase in sterol biosynthesis); 7 = oxathiin (affect mitochondrial transport chain); 9 = anilinopyrimidine (inhibition of amino acid synthesis); 11 = strobilurin type action and resistance (STAR) inhibition mitochondrial respiration; 12 = phenylpyrroles; 14 = aromatic hydrocarbons; 17 = hydroxyanilide; 18 = antibiotics; U= unknown miscellaneous; M = multi-site activity.

[4] Y = use is supported by the registrant, M = use was registered as a User Requested Minor Use Label Expansion (URMULE).

[6] These active ingredients are under re-evaluation (*REV2004-06, PMRA Re-evaluation Program Workplan* (April 2004 to June 2005)).

[7] Re-evaluation of the following products is complete:
- Anilazine (see REV2003-05, not supported by registrant, all uses discontinued)
- Dinocap (see REV2008-02, not supported by registrant, all uses discontinued)
- Dodine (see RVD2008-22)
- Sulfur (see RRD2004-19)
- Metalaxyl and Metalaxyl-M (see PRVD2007-10)
- Vinclozolin (see REV2008-02, not supported by registrant, all uses discontinued)

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY REGISTRANT

Health

Carbendazim

1128807 Determination of contact hypersensitivity in albino guinea pig by the maximization test with R0-17-0099/021-ACR 7073 (quinolate pro fl), DACO: 4.6.6

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