Proposed Registration Decision PRD2011-23

# Oriental Mustard Seed Meal

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# Overview

## Proposed Registration Decision for Oriental Mustard Seed Meal

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of MPT Mustard Seed Meal Technical and MPT Crop Biofumigant, containing the technical grade active ingredient oriental mustard seed meal, to suppress soil-borne nematodes and fungi pathogens on strawberries and caneberries.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of MPT Mustard Seed Meal Technical and MPT Crop Biofumigant.

## What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the PMRA's website at healthcanada.gc.ca/pmra.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act.*

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on oriental mustard seed meal, the PMRA will consider all comments received from the public in response to this consultation document[3]. The PMRA will then publish a Registration Decision[4] on oriental mustard seed meal, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

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

## What Is Oriental Mustard Seed Meal?

Seed meal derived from oriental mustard (*Brassica juncea*) is the leftover seed tissue resulting from the extraction of mustard oil. Oriental mustard seed meal contains high levels of glucosinolates, which hydrolyze into isothiocyanates, volatile compounds chemically related to the active ingredients found in fumigants such as metam sodium (methyl isothiocyanate). Oriental mustard seed meal is the technical grade active ingredient present in MPT Crop Biofumigant, which is used to suppress soil-borne nematodes and fungal pathogens on strawberries and caneberries.

## Health Considerations

### Can Approved Uses of Oriental Mustard Seed Meal Affect Human Health?

**Oriental Mustard Seed Meal is unlikely to affect human health when it is used according to label directions.**

Exposure to oriental mustard seed meal may occur when handling and applying the end-use product, which has a proposed agricultural use as a biofumigant to suppress soil-borne nematodes and fungi pre-planting and post-planting for strawberries and caneberries. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, 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 technical grade active ingredient, oriental mustard seed meal, is of low acute toxicity by the oral and dermal routes, is mildly irritating to the eyes and slightly irritating to the skin. It is a potential respiratory irritant and a skin sensitizer. Mustard is also considered to be a priority allergen by Health Canada. Cautionary statements alerting users to the potential for eye and respiratory irritation, skin sensitization and allergenicity are required on product labels.

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

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

Dermal and inhalation exposure is possible for occupational workers handling or applying the end-use product, MPT Crop Biofumigant, and for post-application workers. Therefore, personal protective equipment is required on the end-use product label to mitigate such exposure concerns. A restricted-entry interval will also be required on the label, restricting access to the treated fields for bystanders and workers for 24 hours after application. Bystander exposure will also be mitigated by keeping unprotected individuals out of the treatment areas for the duration of the treatment period.

Waivers and additional information obtained from the public domain were deemed adequate to address the potential for short-term toxicity, prenatal developmental toxicity, and genotoxicity.

### Residues in Water and Food

**Dietary risks from food and water are not of concern.**

Mustard is used for culinary purposes worldwide, and its degradation product allyl isothiocyanate (AITC) is used as a food additive as a flavouring agent, and as an antispoilage agent. The end-use product, MPT Crop Biofumigant, is not applied directly to food crops, and both oriental mustard seed meal and AITC are expected to rapidly degrade in the soil environment. Therefore, exposure from residues in food is likely to be minimal. Correspondingly, the presence of oriental mustard seed meal and AITC in drinking water is also expected to be negligible. In turn, the PMRA has determined that the establishment of a maximum residue limit is not required for oriental mustard seed meal.

### Occupational Risks From Handling MPT Crop Biofumigant

**Occupational risks are not of concern when MPT Crop Biofumigant is used according to label directions, which include protective measures.**

Occupational exposure to individuals loading or applying MPT Crop Biofumigant is not expected to result in unacceptable risk when the product is used according to label directions.

Precautionary (for example, wearing of personal protective equipment) and hygiene statements on the label are considered adequate to protect individuals from any unnecessary risk due to occupational exposure.

## Environmental Considerations

### What Happens When Oriental Mustard Seed Meal And The Associated End-use Product MPT Crop Bio Fumigant Is Introduced Into the Environment?

Oriental mustard seed meal and the associated secondary compound AITC are derived from a naturally occurring substance. Based on our knowledge of oriental mustard seed meal and AITC, they are not expected to build-up in the environment. When used as per the label directions, as a soil fumigant, the product is expected to pose a minimal risk to non-target organisms.

## Value Considerations

### What Is the Value of MPT Crop Biofumigant?

**MPT Crop Biofumigant is a non-conventional biofumigant that suppresses economically important nematodes and fungal pathogens on strawberries and caneberries.**

Fungal diseases suppressed by MPT Crop Biofumigant include red stele (*Phytophthora fragariae*) on strawberries and phytophthora root rot (*Phytophthora rubi*) on caneberries. Root lesion nematodes (*Pratyclenchus penetrans*) will also be suppressed on both strawberries and caneberries. MPT Crop Biofumigant represents a non-conventional alternative that may improve disease management while reducing the reliance on conventional chemistries.

## Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of MPT Crop Biofumigant to address the potential risks identified in this assessment are as follows.

### Key Risk-Reduction Measures

### Human Health

The signal words "CAUTION – EYE IRRITANT", "POTENTIAL SKIN SENSITIZER" and "WARNING: Contains the allergen mustard" are required on the principal display panels of both the technical and end-use product labels. The statements "May irritate eyes", "May cause respiratory irritation", "Potential skin sensitizer", and "Contains the allergen mustard" are required on the secondary display panel of the technical and end-use product labels.

The personal protective equipment for all applications required on the end-use product label include a long sleeved shirt, chemical-resistant gloves, long pants, shoes and socks, and a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products.

To avoid bystander exposure, the MPT Crop Biofumigant label states that unprotected persons should be kept out of the treated areas for the duration of the treatment period and for 24 hours after watering. To prevent post-application worker exposure to the degradation product AITC, the MPT Crop Biofumigant label requires a restricted-entry interval of 24 hours after watering the product into the soil.

To further reduce the risk of direct application to food crops, directions for use will be revised to state that the incorporation of MPT Crop Biofumigant into the soil layer to a depth of 10 – 15 cm is a necessary step in the application.

## Next Steps

Before making a final registration decision on oriental mustard seed meal, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

## Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on oriental mustard seed meal (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

# Science Evaluation

## Oriental Mustard Seed Meal

## 1.0 The Active Ingredient, Its Properties and Uses

### 1.1 Identity of the Active Ingredient

| | |
|---|---|
| **Active substance** | Oriental mustard seed meal (*Brassica juncea*) |
| **Function** | Fungicide, Nematicide |
| **Chemical name** | |
| **1. International Union of Pure and Applied Chemistry (IUPAC)** | Not applicable. The product is a mixture of complex components |
| **2. Chemical Abstracts Service (CAS)** | Not applicable. The product is a mixture of complex components |
| **CAS number** | Not applicable |
| **Molecular formula** | Not applicable |
| **Molecular weight** | Not applicable |
| **Structural formula** | Not applicable |
| **Purity of the active ingredient** | 100% |

### 1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

### Technical Product—MPT Mustard Seed Meal Technical

| Property | Result |
|---|---|
| Colour and physical state | Yellow brown |
| Odour | Mild mustardy odour |
| Melting range | Not applicable |
| Boiling point or range | Not applicable |
| Specific gravity | 0.62 |
| Vapour pressure at 20°C | Not applicable |
| Henry's law constant at 20°C | Not applicable |
| Ultraviolet (UV)-visible spectrum | Not applicable |
| Solubility in water at 20°C | Not applicable |
| Solubility in organic solvents at 20°C (g/100 mL) | Not applicable |
| *n*-Octanol-water partition coefficient ($K_{OW}$) | Not applicable |

| Property | Result |
|---|---|
| Dissociation constant ($pK_a$) | Not applicable |
| Stability (temperature, metal) | The product is stable, provided it is not exposed to water, an open flame, electrical or static sparks, sparks from welding equipment and strong oxidizers. |

### End-Use Product—MPT Crop Biofumigant

| Property | Result |
|---|---|
| Colour | Yellow brown |
| Odour | Slightly pungent mustard odour |
| Physical state | Solid |
| Formulation type | Pellet (PE) |
| Guarantee | 100% |
| Container material and description | High density polyethylene (HDPE) Plastic bags or jugs, 4 kg – 500 kg |
| Specific gravity | 0.63 |
| pH of 10% dispersion in water | 4.81 |
| Oxidizing or reducing action | The product does not contain any oxidizing or reducing agents. |
| Storage stability | The product is expected to be stable for 12 months when stored in original commercial packaging as per label directions. |
| Corrosion characteristics | The product is not corrosive when stored in the original commercial container as per label directions |
| Explodability | The product does not contain potentially explosive components |

## 1.3 Directions for Use

MPT Crop Biofumigant is to be applied once per season at 980-2240 kg/ha for suppression of red stele on strawberries, phytophthora root rot on caneberries and root lesion nematodes on both strawberries and caneberries. The product is intended for use as part of an integrated pest management program.

In strawberry production, MPT Crop Biofumigant is to be applied directly to the soil surface, 12 to 14 days prior to planting. In caneberry production, MPT Crop Biofumigant may be applied either prior to or after planting, on established plants. In the latter case, the product must be side-dressed between the rows, without touching the plants.

MPT Crop Biofumigant must be incorporated in the upper soil layer to a depth of 10-15 cm and activated by watering. It is recommended that the product be applied in early spring, when soil temperature is still low, but not below 10°C.

### 1.4 Mode of Action

MPT Crop Biofumigant contains 100% seed meal from oriental mustard (*Brassica juncea*), which antagonizes specific fungi and nematodes by a modification of the soil microbial community, interference with nematode reproductive cycles, growth inhibition, feeding deterrence and direct toxicity.

## 2.0 Methods of Analysis

Not applicable for this type of product.

## 3.0 Impact on Human and Animal Health

### 3.1 Toxicology Summary

A detailed review of the toxicological database for oriental mustard seed meal and its degradation product allyl isothiocyanate (AITC) consisting of toxicity studies and waiver rationales was conducted. The scientific quality of the data is acceptable and the database is sufficiently complete to define the majority of the toxic effects that may result from exposure resulting from the intended use of this pest control product.

The applicant submitted acute toxicity (oral, dermal and inhalation), irritation (ocular and dermal), and sensitization studies on oriental mustard seed meal (100 %), and data waiver requests to meet the toxicological evaluation requirements for oriental mustard seed meal. Although the PMRA requires toxicity and irritation studies to be conducted with both the technical grade active ingredient and the end-use product, given that the end-use product is a repack of the technical, and contains no formulants of toxicological concern, testing with the technical grade active ingredient was considered acceptable.

Oriental mustard seed meal was of low acute toxicity by the oral and dermal routes in rats. It was not possible to assess the acute inhalation toxicity of oriental mustard seed meal from the provided study as it was not possible during the experiment to generate an aerosol that would be of respirable size. However, as oriental mustard seed meal is mildly irritating to the eyes, it is assumed that it may be irritating to respiratory mucosa as well. Oriental mustard seed meal was mildly irritating to the eyes and slightly irritating to the skin of rabbits, and is considered a potential skin sensitizer.

Information from the published literature was provided to address the short-term toxicity of oriental mustard seed meal. Several studies were provided, detailing the incorporation of oriental mustard seed meal into the diet of livestock such as dairy cows, chickens and fish, as oriental mustard seed meal is similar in protein content to other feeds such as canola meal. The applicant also cited the GRAS status of mustard, and the extensive and long-term consumption of mustard as a condiment in and on prepared foods, and lack of reports of genotoxicity, mutagenicity or prenatal developmental toxicity, as evidence of its safety.

The main adverse effect reported for mustard in the literature is allergy. Mustard was added to the list of priority food allergens in Canada in 2009. Of the relevant literature evaluated by the review panel, several reports describe severe systemic reactions, including anaphylaxis, following exposure to very small amounts of mustard. It was also concluded that sensitization to mustard can be acquired through dermal and/or respiratory exposure.

The toxicity profile of the degradation product AITC is also relevant to the use of oriental mustard seed meal. A search of publicly available literature indicated that AITC is highly acutely toxic by the oral, dermal and inhalation routes. It is considered to be a severe eye and skin irritant, and some studies have shown skin sensitization potential.

Several short-term studies from the published literature conducted with AITC in rats and mice were reviewed. The main adverse effects seen in these studies were reduced body weight gains and renal dysfunction. The NOAELs, based mainly on the above observations, were determined to be between 10 and 25 mg/kg bw/day.

Three prenatal developmental toxicity studies conducted with AITC, which were reviewed by the European Food Safety Authority (EFSA) Review Panel, were examined. No evidence of developmental toxicity was evident in pregnant rats, hamsters, or rabbits at oral doses of up to 18.5, 23.8 and 12.3 mg/kg bw/day, respectively. However, AITC may be fetotoxic to mice at doses higher than 6.0 mg/kg bw/day, without exhibiting teratogenic effects. Therefore, a dose of 6.0 mg/kg bw/day was considered a NOAEL for the mouse for this endpoint.

Several studies were available in the public domain regarding the mutagenicity of AITC. The EFSA Review Panel reviewed several of these genotoxicity studies conducted with AITC and found both positive and negative results in bacterial and mammalian cells *in vitro*; however, the positive results generally occurred at or near cytotoxic concentrations. The EFSA Review Panel concluded that reactive oxygen species produced may be involved in the genotoxic effects seen in the *in vitro* systems. The results of *in vivo* genotoxicity tests were consistently negative in micronucleus assays in rats and mice, unscheduled DNA synthesis assay in rats, and a dominant lethal mutation assay in mice. Overall, it was concluded that there is no concern with respect to genotoxicity of AITC.

A carcinogenicity bioassay was conducted with AITC by the USA National Toxicology Program. The authors concluded from the results of the rat bioassay that AITC was carcinogenic for male 344/N rats, causing transitional cell papillomas of the urinary bladder. The LOAEL was considered to be 12 mg/kg bw/day based on the significant positive trend seen in the incidence of transitional cell papillomas in urinary bladder of male rats. The study authors concluded from the results of the mouse bioassay that AITC was not carcinogenic for $B6C3F_1$ mice of either sex.

The EFSA Review Panel considered the NOAEL of this study to be 25 mg/kg bw/day.

## 3.2 Food Residue Exposure Assessment

### 3.2.1 Food and Drinking Water

The applicant did not provide residue studies for the end-use product, MPT Crop Biofumigant, or information on the amount of AITC that is expected to be released from oriental mustard seed meal. Information found in the published literature reported that oriental mustard seed meal and the volatile decomposition product, AITC, are expected to rapidly degrade in the soil environment. Accordingly, the presence of oriental mustard seed meal and AITC in drinking water is expected to be negligible.

Food residue exposure to the end-use product is not expected to be of concern as the product is not to be applied directly to the plants, but rather will be applied to the soil prior to seeding or transplanting the crop (strawberries and caneberries) or around mature plants (caneberries only) and then incorporated into the soil layer, for one application in early spring. Minimal contact with aerial portions of the plant or edible plant parts (fruit) is expected to occur. To further reduce the risk of contacting the plant, directions for use will be revised to state that the incorporation of MPT Crop Biofumigant into the soil layer to a depth of 10 – 15 cm is a necessary step in the application, and not only optional for 'optimum results'. Additionally, both oriental mustard seed meal and the degradation product AITC are not expected to persist in the soil. Therefore, the use of MPT Crop Biofumigant is not expected to result in unacceptable dietary risks when the product is used according to label instructions.

### 3.2.2 Maximum Residue Limits (MRLs)

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine the consumption of the maximum amount of residues that are expected to remain on food products when a pesticide is used according to label directions, will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

As the end-use product is not permitted to be applied directly to mature plants, and several mitigation measures are in place to avoid contact with the aerial portions of the plant or edible plant parts, no residues are expected to be present on the fruit, and therefore the PMRA has not required the establishment of a MRL for oriental mustard seed meal.

## 3.3 Occupational and Bystander Risk Assessment

### 3.3.1 Use Description/Exposure Scenario

The proposed agricultural use of MPT Crop Biofumigant is as a biofumigant to suppress soil-borne nematodes and fungi pre-planting and post-planting for strawberries and caneberries. The product is to be applied dry and to a dry soil surface using a calibrated spreader that will

distribute the product uniformly, at a recommended application rate of 9.8 to 22.4 kg MPT Crop Biofumigant per 100 $m^2$ (980 – 2240 kg product/ha). One application is to be made per season, 12 – 14 days prior to seeding or transplanting the crop. Directions for use instruct the user to incorporate the product in the upper soil layer to a depth of 10 – 15 cm using a disc or rotary hoe, and to water the soil immediately after applying MPT Crop Biofumigant. Water should be applied uniformly to the treated area until a soil depth of 10 – 15 cm is well moistened.

For use on established plants, the described use is the same as above with the exception that the product should be applied to the soil around the plant without contacting the plant itself.

### 3.3.2 Mixer, Loader and Applicator Exposure and Risk Assessment

No mixing is required, so there is no occupational risk to mixers.

Occupational exposure to oriental mustard seed meal in MPT Crop Biofumigant is expected to be short term and mainly by the dermal route which is possible during loading and application of the product to the soil. Inhalation of dust from the end-use product is also possible during application. Precautionary statements currently on the proposed product label require the user to wear personal protective equipment (PPE) including a long-sleeved shirt, long pants, shoes and socks. Additional PPE statements that will be required on the label include chemical-resistant gloves, as MPT Crop Biofumigant is considered to be a potential skin sensitizer. Users will also be required to wear a NIOSH approved respirator with any N-95, R-95, P-95 or HE filter for biological products, as oriental mustard seed meal may be irritating to the respiratory mucosa. The use of chemical-resistant gloves and a NIOSH approved respirator will also reduce the risk of an allergic reaction in sensitive individuals. Other precautionary statements on the label will require the user to avoid contact with skin, eyes or clothing, to avoid inhaling or breathing in dust from the product, and to wash hands thoroughly with soap and water after handling.

Significant risk from exposure to MPT Crop Biofumigant for the loader and applicator is not anticipated due to reduced occupational exposure when label directions are followed.

### 3.3.3 Bystander Exposure and Risk Assessment

Bystander exposure is expected to be negligible as the agricultural application of MPT Crop Biofumigant is expected to involve authorized personnel only, and the end-use product label will state that unprotected persons should be kept out of the treated areas for the duration of the treatment period and for 24 hours after watering.

### 3.3.4 Post-Application Exposure

Post-application activity involves application of water to the soil immediately after the end-use product application. Exposure to the end-use product during watering is expected to be negligible as the application of water will be done through commercial irrigation equipment, and therefore no workers will be present in the fields at this time.

To further reduce the risk of worker exposure to oriental mustard seed meal during any other post-application activities, directions for use will state that the incorporation of MPT Crop Biofumigant into the soil layer to a depth of 10 – 15 cm is a necessary step in the application. In addition, due to the formation of AITC upon watering, and the volatile nature of this degradation product, workers may be exposed to AITC in, or volatilizing from, the treated soil. To mitigate risks associated with post-application exposure to AITC, a restricted-entry interval of 24 hours will be required, in the absence of product-specific air concentration data.

### 3.4 Incident Reports Related to Human and Animal Health

Since April 26, 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Health Canada website. As oriental mustard seed meal is not registered for pesticidal use in Canada, there are no incidents reported. Incidents from the United States were searched and reviewed for products containing oriental mustard seed meal for use as pesticides. As of September 8, 2011, there were no health-related incident reports reported by the U.S. EPA or the California Department of Pesticide Regulation for end-use products containing this active ingredient.

## 4.0 Impact on the Environment

### 4.1 Fate and Behaviour in the Environment

When oriental mustard seed meal is exposed to water, the secondary compound AITC is formed, which is considered to impart pesticidal activity. Oriental mustard seed meal and AITC are naturally occuring constituants in plants. Based on our knowledge of these substances, they are not expected to build-up in the enviroment.

### 4.2 Effects on Non-Target Species and Environmental Risk Characterization

When the generation of quantitative data are not practical or apparent risks are considered minimal, a qualitative assessment may be more appropriate. This is considered in the case of non-conventional pest control products, as defined in PRO2010-06, *Guidelines for the Registration of Non-Conventional Pest Control Products*.

In this case, a qualitative environmental risk assessment was conducted for oriental mustard seed meal and the end-use product MPT Crop Biofumigant. Existing information and reviews have indicated that oriental mustard seed meal and AITC do not have adverse effects on non-target organisms, with the exception of certain insects and honey bees where AITC has been shown to be mildly to highly toxic, respectively. The use pattern of the end-use product is to apply it as a pellet on a dry soil surface, incorporate the product in the soil to a depth of 10-15 cm, then water the product into the soil. This use pattern would minimize the product's exposure to birds and mammals, non-target arthropods, non-target plants, and fish and aquatic invertebrates; therefore, environmental risk is expected to be minimal. In addition, a similar registered pest control product and active in the USA do not have any reports of environmental incidents.

# 5.0 Value

## 5.1 Effectiveness Against Pests

### 5.1.1 Acceptable Efficacy Claims

#### 5.1.1.1 Suppression of red stele (*Phytophthora fragariae*) on strawberries

Two strawberry field trials conducted in British Columbia were reviewed. Pre- and post-plant applications of MPT Crop Biofumigant at 1120-2240 kg/ha resulted in a statistically significant reduction of red stele symptoms (chlorosis, vascular discolouration, root rot) under moderate to high disease pressure. Levels of protection corresponded to partial suppression or suppression of the disease. Considering the statically significant disease reductions achieved with oriental mustard seed meal, the large impact of red stele on the Canadian strawberry production, and the need for registered products to manage this important disease, the use of MPT Crop Biofumigant for suppression of red stele on strawberries is supported.

#### 5.1.1.2 Suppression of root lesion nematodes (*Pratylenchus penetrans*) on strawberries

Consistent efficacy trends were noted with MPT Crop Biofumigant in one strawberry field from British Columbia, which was infested with a moderate to high population of root lesion nematodes. In comparison to the untreated control, one pre-plant application at 1120 and 2240 kg/ha provided 89% and 61% reduction of the nematode population, respectively. The product efficacy was confirmed in one greenhouse tomato experiment, where MPT Crop Biofumigant adequately controlled root lesion nematodes in pots containing sandy loam soil, eight weeks after treatment. Based on these efficacy results, the use of MPT Crop Biofumigant for suppression of root lesion nematodes on strawberries is supported.

#### 5.1.1.3 Suppression of phytophthora root rot (*Phytophthora rubi*) and root lesion nematodes (*Pratylenchus penetrans*) on caneberries

Red stele on strawberries and phytophthora root rot on caneberries are caused by two closely related *Phytophthora* species that were recently still considered as variants of *Phytophthora fragariae* (var. *fragariae* and var. *rubi*). These two host-specific pathogen species attack the plant root system and share similar life cycles. Characteristics of root rot development are thus anticipated to be comparable on strawberries and caneberries. These crops are also susceptible to the root lesion nematode.

Based on these similarities, and on the fact that strawberries and caneberries still exhibit a distinct seasonal development and may very well show a different susceptibility to the listed pests, the extrapolation from strawberries to caneberries is supported on a conditional basis. The use of MPT Crop Biofumigant for suppression of phytophthora root rot and root lesion nematodes on caneberries is conditionally supported. Confirmatory data is required in support of the claim of suppression of phytophthora root rot and root lesion nematodes on caneberries.

## 5.2 Phytotoxicity to Host Plants

Phytotoxic symptoms were assessed on strawberry leaves, blossoms and fruit. No adverse effects were observed with pre-plant applications of MPT Crop Biofumigant. In the single trial testing post-plant applications of MPT Crop Biofumigant, phytotoxicity symptoms were observed at all oriental mustard seed meal rates (224, 448, 672 and 896 kg/ha). Phytotoxicity symptoms had disappeared 28 days after treatment. Berry yield, plant growth and plant vigour assessments were not negatively impacted by any oriental mustard seed meal rates. Spotting and necrosis were found exclusively on leaf areas where the pellets remained. However, the product label states that direct contact of the product with the plant must be avoided. Taking these factors into consideration, pre- and post-plant applications of MPT Crop Biofumigant at the proposed rates are not expected to represent an issue with regard to crop tolerance.

## 5.3 Economics

No market analysis was performed for this submission.

## 5.4 Sustainability

### 5.4.1 Survey of Alternatives

Refer to Table 2 of Appendix I for a summary of the active ingredients currently registered for the uses supported with MPT Crop Biofumigant.

### 5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

The use of MPT Crop Biofumigant is compatible with current production practices and is intended for use as part of an integrated pest management program.

### 5.4.3 Information on the Occurrence, or Possible Occurrence, of the Development of Resistance

Based on the multi-site mode of action of oriental mustard seed meal, the risk of disease resistance development is not a major concern for the supported claims.

### 5.4.4 Contribution to Risk Reduction and Sustainability

Red stele, phytophthora root rot and root lesion nematode management in strawberry and caneberry production is generally achieved with pre-plant applications of chemical fumigants such as metam sodium, metam potassium, chloropicrin and 1,3-dichloropropene.

Under the Montreal Protocol on Substances that Deplete the Ozone Layer, the manufacture, import and export of methyl bromide has been prohibited since 2005 in Canada, with the exception of specific critical uses. The fumigant 1,3-dichloropropene has also been voluntarily discontinued by the registrant, with the date of last use of December 31, 2011. This situation further complicates disease management for growers.

In addition, fosetyl-al and metalaxyl are the only two fungicidal active ingredients registered in Canada for control of red stele on strawberries, and metalaxyl-resistant *P. fragariae* isolates have been reported in Canada. MPT Crop Biofumigant is a non-conventional alternative that may improve disease management while reducing the reliance on conventional chemistries.

# 6.0 Pest Control Product Policy Considerations

## 6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e., persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, oriental mustard seed meal and the secondary product, AITC, were considered in accordance with the PMRA Regulatory Directive DIR99-035. The PMRA has reached the following conclusions:

- Oriental mustard seed meal and AITC are not a concern with regard to the Track 1 criteria and are not expected to form any transformation products which would meet the Track 1 criteria. Oriental mustard seed meal and AITC are not expected to build-up or bioaccumulate in the environment.

## 6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use products are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[6]. The list

5 DIR99-03, The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy

6 Canada Gazette, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern and in the order amending this list in the Canada Gazette, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.

is used as described in the PMRA Notice of Intent NOI2005-017 and is based on existing policies and regulations including: DIR99-03; and DIR2006-028, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade oriental mustard seed meal, and the end-use product MPT Crop Biofumigant do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-029.

Oriental mustard seed meal and AITC are derived from a naturally occurring plant substance. Based on our knowledge of these substances, they are not expected to build-up in the environment. Toxicity to most non-target groups is minimal. Based on the use pattern, exposure of oriental mustard seed meal and AITC to all non-target groups will be low.

# 7.0 Summary

## 7.1 Human Health and Safety

The available information for oriental mustard seed meal is adequate to qualitatively identify the toxicological hazards that may result from human exposure to oriental mustard seed meal. Oriental mustard seed meal is of low acute toxicity by the oral and dermal routes, is mildly irritating to the eyes and slightly irritating to the skin. It is a potential respiratory irritant and a skin sensitizer. Mustard is also considered to be a priority allergen by Health Canada.

Occupational exposure to MPT Crop Biofumigant is expected to be minimal if the precautionary statements and recommended personal protective equipment on the product label, which are intended to minimize worker exposure, are observed. Bystander exposure is likely to be negligible. Post-application exposure can be minimized if the required restricted-entry interval is observed by workers and bystanders.

Dietary exposure to oriental mustard seed meal from the use of the proposed end-use product is considered negligible. The PMRA did not establish a MRL for oriental mustard seed meal.

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

8 DIR2006-02, PMRA Formulants Policy.

9 DIR2006-02, PMRA Formulants Policy.

### 7.2 Environmental Risk

Since oriental mustard seed meal is not expected to build-up in the environment and exposure to non-target organisms is expected to be low, risk to the environment through the listed uses will be minimal, and is acceptable.

### 7.3 Value

The data submitted for MPT Crop Biofumigant are adequate to support the use of MPT Crop Biofumigant for suppression of red stele and root lesion nematodes on strawberries. However, confirmatory data is required to support of the claim of suppression of phytophthora root rot and root lesion nematodes on caneberries.

### 7.4 Unsupported Uses

All claims were supported; some with modifications (see Tables 3 and 4 of Appendix 1).

## 8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of MPT Mustard Seed Meal Technical and MPT Crop Biofumigant, containing the technical grade active ingredient oriental mustard seed meal, to suppress soil-borne nematodes and fungi pathogens on strawberries and caneberries.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

# List of Abbreviations

| | |
|---|---|
| % | percent |
| °C | degree(s) Celsius |
| AITC | ally isothiocyanate |
| bw | body weight |
| CAS | Chemical Abstracts Service |
| cm | centimetres |
| DNA | deoxyribonucleic acid |
| EFSA | European Food Safety Authority |
| g | gram |
| GRAS | Generally Recognized as Safe |
| ha | hectare(s) |
| HDPE | high density polyethylene |
| HE | high efficiency |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram |
| $K_{ow}$ | *n*–octanol-water partition coefficient |
| $LD_{50}$ | lethal dose 50% |
| LOAEL | lowest observed adverse effect level |
| $m^2$ | metre(s) squared |
| mg | milligram |
| mL | millilitre |
| MIS | maximum irratation score |
| MRL | maximum residue limit |
| NIOSH | National Institute for Occupational Safety and Health |
| NOAEL | no observed adverse effect level |
| PE | pellet |
| p*K*a | dissociation constant |
| PMRA | Pest Management Regulatory Agency |
| PPE | Personal Protective Equipment |
| TSMP | Toxic Substances Management Policy |
| USA | United States of America |
| U.S. EPA | United States Environmental Protection Agency |
| UV | ultraviolet |
| var. | variation |

# Appendix I Tables and Figures

## Table 1 Summary of Acute Toxicity and Irritative Effects Information for Oriental Mustard Seed Meal (100 %)

| STUDY | SPECIES/STRAIN AND DOSES | RESULT | TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS |
|---|---|---|---|
| Oral toxicity (Limit test)<br><br>Exposure by gavage | Rat – Sprague Dawley<br>(5/sex) | $LD_{50}$ (♀) > 5000 mg/kg bw<br>$LD_{50}$ (♂) > 5000 mg/kg bw<br><br>**Low acute toxicity.** | No mortality occurred. |
| Dermal<br><br>24 hour exposure period | Rat – Sprague Dawley<br>(5/sex) | $LD_{50}$ (♀) > 5000 mg/kg bw<br>$LD_{50}$ (♂) > 5000 mg/kg bw<br><br>**Low acute toxicity.** | No mortality occurred. Erythema occurred at dose sites of all females on Day 1 and/or Day 2. |
| Inhalation | An inhalation study could not be performed as it was not possible to generate an aerosol of respirable size.<br>As the test substance is mildly irritating to the eyes, it is assumed that Oriental mustard seed meal may be irritating to respiratory mucosa as well | | |
| Eye Irritation | Rabbit – New Zealand White<br>(1 male, 2 females)<br><br>Dose: 0.08 – 0.09 g of test substance. Eyes were left unwashed. | MIS = 15.3/110.<br><br>**Mildly irritating.** | Conjunctivitis, iritis, and corneal opacity cleared by 72 hours. |
| Dermal Irritation | Rabbit – New Zealand White<br>(1 male, 2 females)<br><br>Dose: 0.5 g of test substance applied for 4 hours. | MIS = 1.33/8.<br><br>**Slightly irritating.** | Very slight erythema and edema cleared by 48 hours. |
| Dermal Sensitization | Guinea pig – Hartley Albino<br>(males and females) | Non-sensitizing in a Buehler test. | Mustard is considered to be a priority allergen that can cause sensitization from dermal or inhalation exposure. |

## Table 2 Summary of Alternatives for the Uses Supported with MPT Crop Biofumigant

| Crop | Disease | Active ingredient and FRAC Fungicide Group |
|---|---|---|
| Strawberries | Red stele (*Phytophthora fragariae*) | fosetyl-al (U)<br>metalaxyl-M and S-isomer (4)<br>metam sodium (F)<br>metam potassium (F)<br>methyl bromide (F)<br>chloropicrin (F)<br>1-3-dichloropropene (F) |
| | Root lesion nematodes (*Pratylenchus penetrans*) | metam sodium (F)<br>metam potassium (F)<br>methyl bromide (F)<br>1-3-dichloropropene (F) |
| Caneberries | Phytophthora root rot (*Phytophthora rubi*) | metam sodium (F)<br>metam potassium (F)<br>methyl bromide (F)<br>chloropicrin (F) - *raspberries only*<br>1-3-dichloropropene (F) |
| | Root lesion nematodes (*Pratylenchus penetrans*) | metam sodium (F)<br>metam potassium (F)<br>methyl bromide (F)<br>oxamyl (F) - *raspberries only*<br>1-3-dichloropropene (F) |

## Table 3 MPT Crop Biofumigant Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported

| Proposed claim | VSAD supported claim |
|---|---|
| For the control of soil-borne nematodes (such as root-knot, sting, stubby root, lance, lesion and cyst nematodes) and certain soil-borne diseases (such as *Phytopthora*, *Rhizoctonia* and *Verticillium*) on strawberries, apply 980-2240 kg product/ha prior to seeding or transplanting.<br>Maximum number of applications per season: 1 | For the suppression of red stele (*Phytophthora fragariae*) and root lesion nematodes (*Pratylenchus penetrans*) on strawberries, apply 980-2240 kg product/ha prior to seeding or transplanting.<br>Maximum number of applications per season: 1 |

## Table 4 MPT Crop Biofumigant Use (label) Claims Proposed by Applicant and Conditionally Accepted

| Proposed claim | VSAD conditionally supported claim |
|---|---|
| For the control of soil-borne nematodes (such as root-knot, sting, stubby root, lance, lesion and cyst nematodes) and certain soil-borne diseases (such as *Phytopthora*, *Rhizoctonia* and *Verticillium*) on caneberries, apply 980-2240 kg product/ha prior to seeding or transplanting.<br><br>For use on established plants, side-dress the product by spreading 980-2240 kg product/ha without touching the plant.<br><br>Maximum number of applications per season: 1 | For the suppression of phytophthora root rot (*Phytophthora rubi*) and root lesion nematodes (*Pratylenchus penetrans*) on caneberries, apply 980-2240 kg product/ha prior to seeding or transplanting.<br><br>For use on established plants, side-dress the product by spreading 980-2240 kg product/ha without touching the plant.<br><br>Maximum number of applications per season: 1 |

# References

## A. List of Studies/Information Submitted by Registrant

### 1.0 Chemistry

| PMRA Document Number | Reference |
|---|---|
| 1750708 | 2009, 2.11 Manufacturing Process Mustard Seed Meal Diagram, DACO: 2.11, 2.11.1, 2.11.2, 2.11.3, 2.11.4 **CBI** |
| 1750710 | 2009, 2.12 Establishing Certified Limits, DACO: 2.12, 2.12.1 **CBI** |
| 1750711 | 2009, 2.13 Preliminary Analysis, DACO: 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4 **CBI** |
| 1750712 | 2008, 2 Analysis of Product Mustard Seed Meal, DACO: 2.13, 2.13.1, 2.13.2, 2.13.3, 2.13.4 **CBI** |
| 1750713 | 2009, Analysis Report, DACO: 2.14 **CBI** |
| 1750714 | 2009, Part 2 TGAI and Part 3 EP chemistry - key to products used, DACO: 2.14 **CBI** |
| 1750715 | 2009, 2.14 Chemical and Physical Properties, DACO: 2.14 **CBI** |

### 2.0 Human and Animal Health

| PMRA Document Number | Reference |
|---|---|
| 1804922 | 2009, Summary – Acute Toxicology Profile of Oriental mustard seed meal, DACO 4.0. |
| 2078926 | 2002, Acute Oral Toxicity of Oriental Mustard Seed Meal, DACO 4.2.1. |
| 2078927 | 2002, Acute Dermal Toxicity of Oriental Mustard Seed Meal, DACO 4.2.2. |
| 2078928 | 2002, Acute Inhalation Toxicity of Oriental Mustard Seed Meal, DACO 4.2.3. |
| 2078929 | 2002, Primary Eye Irritation Study with Oriental Mustard Seed Meal, DACO 4.2.4. |
| 2078930 | 2002, Primary Dermal Irritation Study with Oriental Mustard Seed Meal, DACO 4.2.5. |
| 2078931 | 2002, Dermal Sensitization Study with Oriental Mustard Seed Meal, DACO 4.2.6. |
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1750730 US EPA Biopesticides Registration Action Document: Oriental Mustard Seed (OMS), 2008. DACO 12.5.

ChemIDPlus/HSDB/NTP Toxicity of allyl isothiocyanate (CASRN 57-06-7).

## 3.0 Environment

| PMRA Document Number | Reference |
|---|---|
| 1804923 | 2009, Summaries, environmental chemistry and fate of mustard seed meal, DACO: 8.1 |
| 1804924 | 2009, Summaries, environmental toxicity of mustard seed meal, DACO: 9.1, 9.2.4.1, 9.2.4.2, 9.2.4.3, 9.2.5, 9.2.6, 9.2.7, 9.3.2, 9.5.2.1, 9.5.2.2, 9.5.2.3, 9.6.2.1, 9.6.2.2, 9.6.2.3, 9.6.2.4, 9.6.2.5, 9.6.2.6, 9.8.4 |
| 1750729 | 2009, Comprehensive Mustard Seed Summary Mustard Seed Meal Technical, DACO: 12.7 CBI |
| 1750730 | 2009, Biopesticides Registration Action Document, Oriental mustard seed (OMS). PC Code 014921. US environmental protection agency, office of pesticide programs, biopesticide and pollution prevention division. DACO: 12.5 CBI |

## 4.0 Value

| PMRA Document Number | Reference |
|---|---|
| 1848636 | 2009, Evaluation of Mustard Meal for Control or Suppression of Red Stele Root Rot, Root Lesion Nematodes and Weeds in Strawberry, DACO: 10.2.3, 10.2.3.3 |
| 1848638 | 2009, Mustard Meal for Suppression of Phytopthora Red Stele Root Rot in Strawberry, DACO: 10.2.3, 10.2.3.3 |

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1945552 2009, Mustard Meal for Pre-plant Suppression of Root Lesion and Root Knot Nematode in Strawberry, DACO: 10.2.3, 10.2.3.3

## B. Additional Information Considered

### i) Published Information

#### 1.0 Human and Animal Health

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