Proposed Registration Decision PRD2012-11

# Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites

*(publié aussi en français)*

**25 April 2012**

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

Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6604-E2
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

Canada

ISSN: 1925-0878 (print)
1925-0886 (online)

Catalogue number: H113-9/2012-11E (print version)
H113-9/2012-11E-PDF (PDF version)

**© Her Majesty the Queen in Right of Canada, represented by the Minister of Health Canada, 2012**

All rights reserved. No part of this information (publication or product) may be reproduced or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, or stored in a retrieval system, without prior written permission of the Minister of Public Works and Government Services Canada, Ottawa, Ontario K1A 0S5.

# Table of Contents


Overview ..... 1
Proposed Registration Decision for Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites ..... 1
What Does Health Canada Consider When Making a Registration Decision? ..... 1
What Are Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites? ..... 2
Health Considerations ..... 2
Environmental Considerations ..... 4
Value Considerations ..... 4
Measures to Minimize Risk ..... 4
Next Steps ..... 5
Other Information ..... 5
Science Evaluation ..... 7
1.0 The Active Ingredient, Its Properties and Uses ..... 7
1.1 Identity of the Active Ingredient ..... 7
1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product ..... 8
1.3 Directions for Use ..... 9
1.4 Mode of Action ..... 9
2.0 Methods of Analysis ..... 9
2.1 Methods for Analysis of the Active Ingredient ..... 9
2.2 Method for Formulation Analysis ..... 9
3.0 Impact on Human and Animal Health ..... 10
3.1 Toxicology Summary ..... 10
3.1.1 Incident Reports ..... 10
3.2 Food Residue Exposure Assessment ..... 11
3.3 Occupational and Residential Risk Assessment ..... 11
3.3.1 Use Description / Exposure Scenario ..... 11
3.3.2 Mixer, Loader and Applicator Exposure and Risk Assessment ..... 11
3.3.3 Bystander Exposure and Risk Assessment ..... 11
3.3.4 Postapplication Exposure ..... 12
4.0 Impact on the Environment ..... 12
4.1 Fate and Behaviour in the Environment ..... 12
4.2 Environmental Risk Characterization ..... 12
4.2.1 Risks to Terrestrial Organisms ..... 12
4.2.2 Risks to Aquatic Organisms ..... 13
4.2.3 Incident Reports ..... 14
5.0 Value ..... 14
5.1 Effectiveness Against Pests ..... 14
5.1.1 Acceptable Efficacy Claims ..... 14
5.2 Economics ..... 18

5.3 Sustainability ..... 18
5.3.1 Survey of Alternatives ..... 18
5.3.2 Compatibility with Current Management Practices Including Integrated Pest Management ..... 18
5.3.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance ..... 18
5.3.4 Contribution to Risk Reduction and Sustainability ..... 18
6.0 Pest Control Product Policy Considerations ..... 18
6.1 Toxic Substances Management Policy Considerations ..... 18
6.2 Formulants and Contaminants of Health or Environmental Concern ..... 19
7.0 Summary ..... 20
7.1 Human Health and Safety ..... 20
7.2 Environmental Risk ..... 20
7.3 Value ..... 20
7.4 Unsupported Uses ..... 21
8.0 Proposed Regulatory Decision ..... 21
List of Abbreviations ..... 23
Appendix I Tables and Figures ..... 25
Table 1 Toxicity Profile of Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphite and Its Associated End-use Product (Phostrol Fungicide) ..... 25
Table 2 Short-term Toxicity, Prenatal Development Toxicity, and Genotoxicity of Technical Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites ..... 29
Table 3 Summary of Fungicide Alternatives for the Uses Supported with Phostrol Fungicide ..... 30
Table 4 Phostrol Fungicide Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported ..... 32
References ..... 35

# Overview

## Proposed Registration Decision for Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites

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 Phostrol 53.6% Fungicide and Phostrol Fungicide, containing the technical grade active ingredient mono- and dibasic sodium, potassium and ammonium phosphites, to suppress or control several fungal diseases on a variety of vegetable and berry crops, as well as outdoor and indoor ornamentals and turf.

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 Phostrol 53.6% Fungicide and Phostrol Fungicide.

## 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 (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants).

---

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."

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 Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on mono- and dibasic sodium, potassium and ammonium phosphites, 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 mono- and dibasic sodium, potassium and ammonium phosphites, 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 Are Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites?

Mono- and dibasic sodium, potassium and ammonium phosphites are salts of phosphorous acid. These fungicide active ingredients belong to the Group 33 of the Fungicide Resistance Action Committee and are classified as phosphonates. The mode of action of mono- and di-basic sodium, potassium and ammonium phosphites is both indirect and direct, and involves the induction of host plant resistance and the inhibition of oxidative phosphorylation.

## Health Considerations

### Can Approved Uses of Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites Affect Human Health?

**Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites are unlikely to affect human health when used according to label instructions.**

Exposure to mono- and dibasic sodium, potassium, and ammonium phosphites may occur when handling and applying the product. 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.

Mono- and dibasic sodium, potassium, and ammonium phosphites are of low toxicity by the oral, dermal and inhalation routes, minimally irritating to the eyes, and mildly irritating to the skin.

---

[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*.

The available information suggests that it is unlikely to have any short-term or prenatal developmental effects, as well as any significant genotoxic effects. The precautionary label statement indicating that contact with skin, eyes, and clothing must be avoided, and the personal protective equipment statement that applicators and other handlers must wear a long-sleeved shirt, long pants, gloves, shoes plus socks, and protective eyewear are effective mitigative measures to reduce the risk associated with the use of mono- and dibasic sodium, potassium, and ammonium phosphites.

## Residues in Water and Food

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

Dietary risk to humans is considered negligible based on the intended use, long history of use, and low toxicity of the end-use product. The available literature suggests that there is no toxicological concern from ingestion of the end-use product residues.

It is anticipated that the use of mono- and dibasic sodium, potassium, and ammonium phosphites in Canada on food crops will not pose a risk to any segment of the population, including infants, children, adults and seniors, when the foods are subjected to the normal process of washing, peeling and cooking for human consumption. In the United States, phosphorous acid has been designated Generally Regarded as Safe (GRAS) and the potassium salts of phosphorous acid have been exempted from the requirement of tolerance in and on all food commodities when used as an agricultural fungicide on food crops. The United States Environmental Protection Agency (USEPA) introduced an initiative whereby an exemption from the requirement of tolerance was established for ammonium, sodium, and potassium salts of phosphorous acid on all food commodities to permit post-harvest application to stored potatoes at 35,600 ppm or less of phosphorous acid.

Although this end-use product will be used for agricultural crops outdoors, as well as in contained treatment areas, it is not to be applied near or directly to water. No risk due to exposure from drinking water is anticipated.

## Risks in Residential and Other Non-Occupational Environments

**Bystander exposure is possible from spray drift, but exposure is expected to be negligible if the precautionary label statements are observed.**

Precautionary statements (for example, ensuring that the potential for spray drift to areas of human habitation is minimal) on the label of Phostrol Fungicide are considered adequate to protect individuals, children and pets from exposure due to incidental contact with this product.

### Occupational Risks From Handling Phostrol Fungicide

**Occupational exposure to individuals mixing, loading, or applying Phostrol Fungicide 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 occupational exposure.

## Environmental Considerations

### What happens when mono- and dibasic sodium, potassium and ammonium phosphites are introduced into the environment?

The end-use product Phostrol Fungicide, containing mono- and dibasic sodium, potassium and ammonium phosphites, enters the environment when it is sprayed on various crops by in-furrow treatment, ground or aerial applications. It is not expected that mono- and dibasic sodium, potassium and ammonium phosphites will pose a risk to non-target terrestrial and aquatic species given its low toxicity to these organisms.

## Value Considerations

### What Is the Value of Phostrol Fungicide?

**Phostrol Fungicide is a non-conventional alternative fungicide with systemic properties that may be integrated in a spray program for suppression or control of several diseases on a wide range of crops.**

Major diseases suppressed or controlled by Phostrol Fungicide include phytophthora root rot on raspberries, late blight and pink rot on potatoes as well as downy mildew on grapes. Phostrol Fungicide also has a low risk of resistance development, which makes it a viable option for the management of certain high-risk pathogens.

## 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 Phostrol Fungicide to address the potential risks identified in this assessment are as follows.

**Key Risk-Reduction Measures**

**Human Health**

Because mono- and dibasic sodium, potassium, and ammonium phosphites are used for formulating a commercial product, the statement in the precaution section on the Phostrol 53.6% Fungicide label, “prevent access by unauthorized personnel”, will help mitigate the inappropriate use of the product, and help avoid exposure. Other precautionary statements on the technical and end-use product labels, such as: “avoid breathing vapors or spray mist, avoid contact with eyes; remove contaminated clothing and wash clothing before use; applicators and other handlers must wear protective eyewear, long pants and long sleeved shirt, waterproof gloves, and shoes plus socks,” should be effective in minimizing the potential for exposure.

## Next Steps

Before making a final registration decision on mono- and dibasic sodium, potassium and ammonium phosphites, 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 mono- and dibasic sodium, potassium and ammonium phosphites (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

## Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites (Phostrol)

## 1.0 The Active Ingredient, Its Properties and Uses

### 1.1 Identity of the Active Ingredient

| | |
|---|---|
| **Active substance** | Mono- and dibasic sodium, potassium and ammonium phosphites |
| **Function** | Fungicide |
| **Chemical name** | |
| **1. International Union of Pure and Applied Chemistry (IUPAC)** | 1. Diammonium hydrogen phosphite<br>2. Dipotassium hydrogen phosphite<br>3. Disodium hydrogen phosphite<br>4. Ammonium dihydrogen phosphite<br>5. Potassium dihydrogen phosphite<br>6. Sodium dihydrogen phosphite |
| **2. Chemical Abstracts Service (CAS)** | 1. Phosphonic acid, diammonium salt<br>2. Phosphonic acid, dipotassium salt<br>3. Phosphonic acid, disodium salt<br>4. Phosphonic acid, monoammonium salt<br>5. Phosphonic acid, monopotassium salt<br>6. Phosphonic acid, monosodium salt |
| **CAS number** | 1. 51503-61-8 (hydrated form)<br>2. 13492-26-7<br>3. 13708-85-5<br>4. 13446-12-3<br>5. 13977-65-6<br>6. 13933-52-3 |
| **Molecular formula** | 1. $(NH_4)_2HPO_3$<br>2. $K_2HPO_3$<br>3. $Na_2HPO_3$<br>4. $(NH_4)H_2PO_3$<br>5. $KH_2PO_3$<br>6. $NaH_2PO_3$ |
| **Molecular weight** | Not applicable as the product is a mixture of six components |
| **Structural formula** | Not applicable as the product is a mixture of six components |
| **Purity of the active ingredient** | 53.6% |

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

### Technical Product—Phostrol 53.6% Fungicide

| Property | Result |
|---|---|
| Colour and physical state | Gardner 3 as a clear liquid |
| Odour | No discernable odour |
| Melting range | Not applicable, the product is a liquid |
| Boiling point or range | Not available |
| Specific gravity | 1.40 – 1.43 |
| Vapour pressure at 20°C | Expected to be negligible. |
| Ultraviolet (UV)-visible spectrum | Not likely to absorb at $\lambda > 300$ nm |
| Solubility in water at 20°C | Highly soluble in water |
| Solubility in organic solvents at 20°C (g/100 mL) | Not available |
| *n*-Octanol-water partition coefficient ($K_{ow}$) | Not applicable, the product is inorganic |
| Dissociation constant ($pK_a$) | No dissociable groups present. |
| Stability (temperature, metal) | Corrosivity is expected to be negligible towards stainless steel over the time frame required for manufacture of the product |

### End-Use Product—Phostrol Fungicide

| Property | Result |
|---|---|
| Colour | Gardner 3 |
| Odour | No discernible odour |
| Physical state | Clear liquid |
| Formulation type | Liquid |
| Guarantee | 53.6% |
| Container material and description | HDPE Plastic bottles/totes (0.1 to 1050 kg) |
| Specific gravity at 20°C | 1.40 – 1.43 |
| pH of 1% dispersion in water | 6.5 – 7.5 |
| Oxidizing or reducing action | Incompatible with strong oxidizers |
| Storage stability | No significant change in phosphite content after storage under warehouse conditions in plastic containers for two years |

| Property | Result |
|---|---|
| Corrosion characteristics | No observable corrosion in the commercial packaging |
| Explodability | The product is not explodable |

### 1.3 Directions for Use

Depending on the targeted crop, Phostrol Fungicide is to be applied preventatively as a foliar, drench, in-furrow or post-harvest treatment. Applications should begin when conditions favouring disease development exist and continue throughout the season at specified intervals. Tank-mixes with conventional fungicides are proposed on certain crops.

Four to seven foliar applications are recommended on most supported crops at rates between 2.9-11.6 L/ha in sufficient water volume to provide thorough coverage (200-1000 L water/ha). The aerial application of Phostrol Fungicide is exclusively for use on potatoes. In-furrow and post-harvest treatments are for pink rot and late blight management on potatoes. Drench applications are for use against phytophthora root rot on greenhouse-grown and outdoor bedding plants, potted plants and cut flowers.

### 1.4 Mode of Action

Phostrol Fungicide contains 53.6% mono- and dibasic sodium, potassium and ammonium phosphites. The mode of action of Phostrol Fungicide involves the induction of host plant resistance and the inhibition of oxidative phosphorylation.

Phosphite fungicides such as Phostrol Fungicide are defined as products made up of the salts and esters of phosphorous acid. The dissociated phosphite ions are known to play a significant role in the antifungal activity of phosphite fungicides.

## 2.0 Methods of Analysis

### 2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Phostrol 53.6% Fungicide have been validated and assessed to be acceptable for the determinations.

### 2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in Phostrol Fungicide has been validated and assessed to be acceptable for use as an enforcement analytical method.

# 3.0 Impact on Human and Animal Health

## 3.1 Toxicology Summary

The PMRA has conducted a detailed review of the submitted data for mono- and dibasic sodium, potassium, and ammonium phosphites. The submitted toxicity studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is adequate to assess the toxicological hazards of this pest control product.

Submitted information for the technical grade active ingredient, mono- and dibasic sodium, potassium, and ammonium phosphites, and the end-use product, Phostrol Fungicide (53.6 % w/w mono- and dibasic sodium, potassium, and ammonium phosphites), suggests that the active ingredient is of low acute toxicity by the oral, dermal, and inhalation routes of exposure. Mono- and dibasic sodium, potassium, and ammonium phosphites are mildly irritating to the skin, minimally irritating to the eyes, and is not a skin sensitizer.

Based on information for short-term toxicity, developmental toxicity (prenatal), and genotoxicity available for mono- and dibasic sodium, potassium, and ammonium phosphites at the time of evaluation, in addition to a long history of safe use as an agrochemical pesticide in Australia and the United States, it appears unlikely that treatment-related effects will result from exposure to mono- and dibasic sodium, potassium, and ammonium phosphites.

The mutagenicity of mono- and dibasic sodium, potassium, and ammonium phosphites was assessed with the reverse gene mutation assay in bacteria (Ames assay). *Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537, *E. Coli, and Saccharomyces cereviscae* were exposed to aluminum tris(ethyl phosphite), a phosphite based surrogate compound reviewed in support of the genotoxicity data requirements for mono- and dibasic sodium, potassium, and ammonium phosphites. The findings were negative in that there was no evidence of a treatment-related response over background.

A summary of the toxicology information provided can be found in Appendix 1, Tables 1 and 2.

### 3.1.1 Incident Reports

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 Health Canada's website. Incidents from Canada were searched and reviewed for active mono- and dibasic sodium, potassium, and ammonium phosphites. As of February 4, 2011, there have been no human incident reports for products containing mono- and dibasic sodium, potassium, and ammonium phosphites in Canada.

## 3.2 Food Residue Exposure Assessment

Due to the low toxicity of mono- and dibasic sodium, potassium, and ammonium phosphite, and its long history of use as an agrochemical, no adverse effects are anticipated from the presence of residues on food.

In the United States, phosphorous acid is classified by the Food and Drug Administration as Generally Regarded as Safe (GRAS). The salts of phosphorous acid have been exempted from the requirement of tolerance in, and on, all food commodities when used as an agricultural fungicide on food crops.

Since there is a reasonable certainty that no harmful effects will result from dietary exposure to residues of mono- and dibasic sodium, potassium, and ammonium phosphites based on the low levels of toxicity and the long history of safe use, the PMRA has not required the establishment of a maximum residue limit for mono- and dibasic sodium, potassium, and ammonium phosphites.

## 3.3 Occupational and Residential Risk Assessment

### 3.3.1 Use Description / Exposure Scenario

Phostrol Fungicide is proposed to control or suppress several diseases, including phytophthora and pythium root rot, late blight and downy mildew on terrestrial food crops, forests and foodlots, greenhouse non-food crops, outdoor ornamentals, and turf. Airblast, ground boom, aerial, custom ground, in-furrow, post harvest and hand gun applications have been proposed.

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

Mixing with water is required while continuously agitating the solution. This procedure is typical and has the potential for skin and eye exposure, *i.e.* principally dermal exposure but there is the potential for splash and, thus, the potential for ocular exposure exists. While applying Phostrol Fungicide, there is the potential for dermal, ocular, and inhalation exposure to the workers as well as any bystanders in the immediate area. Exposure to individuals mixing, loading, and applying the pesticide, as well as those involved with clean-up and maintenance duties, is expected to be negligible when the product is used according to label directions.

### 3.3.3 Bystander Exposure and Risk Assessment

Bystander exposure (including children and pets) is expected to be negligible when the product is used according to label directions. The end-use product label instructs users to not apply product under windy conditions, thereby limiting bystander exposure from possible spray drift.

### 3.3.4 Postapplication Exposure

Postapplication activities are typical, *for example,* harvesting. A re-entry period of 12 hours is proposed for Phostrol Fungicide for all proposed uses with the exception of turf. Areas of treated turf may be re-entered when the pesticide spray solution dries.

Observing the re-entry interval and hygiene statements on the label is sufficient to limit individuals from unnecessary risk due to postapplication exposure.

## 4.0 Impact on the Environment

### 4.1 Fate and Behaviour in the Environment

Phosphorous acid and its phosphite salts are rapidly dissociated in the environment to yield hydrogen and phosphite ions. Over time, the phosphite ions can be systemically taken up by plants as various salts, transformed in soil to different oxidation states such as phosphate, or bound up with other substances in soil. Phosphites will eventually convert to phosphates via microbial transformation in soil, but the process is very slow. Phosphite ions are miscible in water and are, thus, subject to being removed from the soil by runoff and leaching.

### 4.2 Environmental Risk Characterization

When the generation of quantitative data for non-conventional pest control products are not practical or apparent risks are considered minimal, a qualitative assessment may be more appropriate. For the risk assessment of Phostrol Fungicide, both qualitative and quantitative approaches were used.

Toxicity studies with mono- and dipotassium salts of phosphorous acid were submitted as surrogate data for bobwhite quail, rainbow trout, *Daphnia magna*, and the honeybee. This was considered acceptable as the results should reflect the toxicity due to the phosphite ion, which is the moiety of interest for this assessment. Other published information was used to assess the potential for effects on terrestrial plants and algae.

### 4.2.1 Risks to Terrestrial Organisms

Phosphite was found to be practically non-toxic to the bobwhite quail (i.e., $LD_{50}$ greater than 2000 mg a.i./kg bw for the acute oral toxicity, and $LC_{50}$ greater than 5000 mg a.i./kg dw diet for the avian dietary) and the honey bee (i.e., $LD_{50}$ greater than 11 µg a.i./bee [or 12.3 kg a.i./ha]). As such, the risk to these non-target organisms is considered to be minimal.

Although the phytotoxicity of phosphite has been identified (and well-documented in public literature) as a potential concern in phosphorous-depleted soils, the risks under the proposed use of Phostrol Fungicide are considered to be minimal. A lack of incidents reporting toxicity to terrestrial plants and a history of use in agriculture as either a fertilizer or fungicide in other countries (USEPA Ecological Incident Information System (EIIS) database) and Canada, supports this conclusion. Risk to non-target terrestrial plants is expected to be minimal.

### 4.2.2 Risks to Aquatic Organisms

Phosphite was found to be practically non-toxic ($LC_{50}$ greater than 100 mg a.i./L) to the rainbow trout and slightly toxic ($LC_{50}$ ranging from 10 to 100 mg a.i./L) to *Daphnia magna*.

As is seen for terrestrial plants, phosphites could also potentially inhibit the growth of certain algae in phosphorous-depleted environments. This may be, in part, due to the variability in how phosphites are utilized by freshwater or marine algae. In general, however, risk to algae from the use of Phostrol Fungicide is expected to be minimal.

Using a conservative scenario of seven ground applications of 11.6 L/ha (6.2 L a.i./ha) for potatoes, with no dissipation between the applications, the estimated environmental concentration (EEC) in an 80-cm deep water system is equal to 3.88 mg a.i./L. A screening-level aquatic risk assessment was conducted with the most sensitive species. No definitive toxicity values were available; however, the most conservative toxicity classification from the USEPA review was “slightly toxic” for freshwater invertebrates. The lower end of the range defining the classification “slightly toxic” is 10 mg a.i./L. Using an uncertainty factor of 2 (i.e. 5 mg a.i./L), the screening-level risk quotient is 0.78. The level of concern (LOC = 1) is not exceeded.

For an assessment of risk to amphibians, the EEC in a 15-cm deep water system is equal to 20.67 mg a.i./L (using a density of 1.4 g/L for Phostrol 53.6% Fungicide). When this EEC is compared to the lowest toxicity value of 100 mg a.i./L for the surrogate species rainbow trout (taken from the lower end of the range defining a classification of pratically non-toxic, $LC_{50}$ value of greater than 100 mg a.i./L) and using a uncertainty factor of 2 (i.e. 50 mg a.i./L), the screening-level risk quotient is 0.41. The level of concern is not exceeded.

Thus, it is unlikely that there will be a potential for adverse effects of Phostrol Fungicide on non-target aquatic organisms from spray drift or runoff events to water systems close to sprayed sites.

Overall, it is unlikely that exposure to mono- and dibasic sodium, potassium, and ammonium phosphites and the end-use product Phostrol Fungicide will have any adverse effects on non-target terrestrial and aquatic organisms. As such, the risk associated with the use of this end-use product at the proposed application rates is expected to be minimal.

### 4.2.3 Incident Reports

No incidents are reported in the USEPA Ecological Incident Information System (EIIS) database for mono- and dibasic sodium, potassium, and ammonium phosphites (USEPA OPP Chemical Code 076002) used as a fungicide. As for other registered end-use products containing phosphites, only two phytotoxicity cases were reported in the early 2000's for Aluminum tris O-ethyl phosphonate [Fosetyl-Al] **(**USEPA OPP Chemical Code 123301). These reports are considered to be not relevant for this assessment of Phostrol Fungicide.

## 5.0 Value

### 5.1 Effectiveness Against Pests

Information was provided in the form of use history information and 45 field trials testing Phostrol Fungicide (22 trials) or related phosphite fungicides (23 trials). The guarantee of phosphite fungicides is often expressed in phosphorous acid equivalents (PAE) since this is the fraction that is responsible for fungicide activity. The concept of PAE has been used in this review. However, in trials where other phosphite products were used, significant variability was observed among the fungicides at equivalent PAE rates. Consequently, surrogate trial data using products other than Phostrol Fungicide was considered as supplementary.

### 5.1.1 Acceptable Efficacy Claims

#### 5.1.1.1 Suppression of downy mildew (*Peronospora parasitica*) on head and stem brassicas (Crop Subgroup 5A)

Two trials were conducted on Chinese broccoli and broccoli in support of the proposed claim. Phostrol Fungicide applied three times at the proposed rates resulted in statistically similar disease control as the commercial standards, but fungicides did not perform up to the expected efficacy standards for disease control. Six supplementary trials tested phosphite fungicides against downy mildew on cabbage, collard, mustard greens and Chinese broccoli. Phosphite fungicides showed a substantial antifungal activity on various head and stem brassica crops. Based on these results, the use of Phostrol Fungicide is accepted for suppression of downy mildew on head and stem brassica crops at the proposed rates, however, confirmatory data are required.

#### 5.1.1.2 Suppression of phytophthora root rot (*Phytophthora* spp.) on raspberries

Use history information from three reports outlined the value of Phostrol Fungicide in managing phytophthora root rot on raspberries. Given the lack of efficacy trials and the statement that a lower efficacy was observed in comparison to a commercial standard, the use of Phostrol Fungicide is accepted for suppression of phytophthora root rot on raspberries at the proposed rate, however, confirmatory data are required.

#### 5.1.1.3 Suppression of downy mildew (*Pseudoperonospora cubensis*) on cucurbit vegetables (Crop Group 9)

In two cucumber trials, preventative applications of Phostrol Fungicide statistically reduced downy mildew under low disease pressure at the beginning of the growing season. When tank-mixed with chlorothalonil, Phostrol Fungicide statistically increased levels of protection when compared to chlorothalonil alone. The use of Phostrol Fungicide is accepted for suppression of downy mildew on cucurbit vegetables at the proposed rates based on biological similarities among the crop group, however, confirmatory data are required.

#### 5.1.1.4 Control of downy mildew (*Plasmopara viticola*) on grapes

In two trials, four applications of Phostrol Fungicide at the proposed rates adequately controlled downy mildew on grapes. Phostrol Fungicide was statistically comparable to the commercial standards in terms of efficacy. The use of Phostrol Fungicide is accepted for control of downy mildew on grapes at the proposed rates.

#### 5.1.1.5 Control of downy mildew (*Bremia lactucae*) on head and leaf lettuce, upland cress, endive and radicchio

Three lettuce trials were provided in support of the proposed claim. Phostrol Fungicide, at the proposed rates, consistently controlled downy mildew on lettuce. The use of Phostrol Fungicide for control of downy mildew is accepted at the proposed rates on lettuce. The use on lettuce can be extrapolated to endive, radicchio and upland cress based on similarities in disease development and production practices.

#### 5.1.1.6 Control of late blight (*Phytophthora infestans*) on potatoes - foliar applications

Eight potato trials were provided in support of the proposed claim. Two trials tested eight foliar applications of Phostrol Fungicide at the lower proposed rate against potato late blight; foliar blight was statistically reduced by an average of 83%. Phostrol Fungicide at the higher proposed rate generally resulted in adequate disease control under moderate to high disease pressure. Based on the weight of evidence, the use of Phostrol Fungicide for control of potato late blight at 2.9-11.6 L/ha is accepted.

#### 5.1.1.7 Control of late blight (*Phytophthora infestans*) on potatoes - post-harvest treatment

Four trials were submitted in support of the proposed claim. After 21 days of storage, Phostrol Fungicide applied once at the proposed rate resulted in adequate disease control under moderate disease pressure. In two trials conducted under severe disease pressure, Phostrol Fungicide at the proposed rate provided complete post-harvest control of potato late blight after one month of storage. One post-harvest application of Phostrol Fungicide at the proposed rate (0.42 L in 2L water to 1 tonne tubers) is accepted for control of potato late blight.

#### 5.1.1.8 Suppression of pink rot (*Phytophthora erythroseptica*) on potatoes - foliar applications

Foliar applications of Phostrol Fungicide against potato pink rot were tested in seven trials. The lower proposed rate of 2.9 L/ha was not tested in the pink rot studies, the rate of 5.8 L/ha suppressed the disease when applied twice, and inconsistent results were achieved with the rate of 11.6 L/ha. Therefore, the use of Phostrol Fungicide is accepted for suppression of potato pink rot at 5.8-11.6 L/ha. Applications at these rates will also cover potato late blight.

#### 5.1.1.9 Suppression of pink rot on potatoes - in-furrow application

One trial tested one in-furrow spray of Phostrol Fungicide at 4.7 L/ha under low disease pressure, which resulted in a substantial reduction of potato pink rot. Field studies had previously shown that foliar applications of Phostrol Fungicide do supress pink rot on potatoes. Consequently, an in-furrow application of Phostrol Fungicide at planting is accepted for suppression of potato pink rot, however, confirmatory data are required. The product is to be applied at the same rates supported for foliar applications, i.e. 5.8-11.6 L/ha.

#### 5.1.1.10 Control of pink rot (*Phytophthora erythroseptica*) on potatoes - post-harvest treatment

Four trials were submitted in support of the proposed claim. After 21 days of storage, Phostrol Fungicide provided an average of 91% disease reduction under high disease pressure. In two trials conducted under severe disease pressure, Phostrol Fungicide at the proposed rate provided complete post-harvest control of pink rot after one month of storage. One post-harvest application of Phostrol Fungicide (0.42 L in 2L water to 1 tonne tubers) is accepted for control of potato pink rot.

#### 5.1.1.11 Aerial applications on potatoes

Based on the use history information from the applicant and the need for aerial applications for potato late blight management under wet weather conditions, the aerial use of Phostrol Fungicide for control of potato late blight and pink rot is accepted, however, confirmatory data are required.

#### 5.1.1.12 Control of leather rot (*Phytophthora cactorum*) on strawberries

One trial was conducted on strawberry leather rot under moderate disease pressure. Four applications of Phostrol Fungicide at 4.1 L/ha resulted in 92% reduction of necrotic fruit clusters and an average of 54% reduction of disease severity at harvest. Use history information from a US strawberry production guide provided further evidence of Phostrol's activity on *Phytophthora cactorum*. The use of Phostrol Fungicide is accepted at 4.1 L/ha for control of leather rot on strawberries; however, confirmatory data are required.

#### 5.1.1.13 Suppression of late blight (*Phytophthora infestans*) on tomato crops (Crop Subgroup 8-09A)

Considering that 1) *Phytophthora infestans* is the causal agent of late blight on potatoes and tomatoes, 2) late blight develops similarly on their foliage, and 3) these two solanaceaeous crops have comparable biology in the field, the use of Phostrol Fungicide for late blight management may be extrapolated from potatoes to tomatoes. Since a rate of 2.9-11.6 L/ha was accepted for foliar control of potato late blight, the proposed rate range (2.9-5.8 L/ha) is expected to suppress the disease on the tomato crop subgroup.

#### 5.1.1.14 Suppression of phytophthora root rot on greenhouse-grown and outdoor bedding plants, potted plants and cut flowers

Three nursery trials tested foliar applications of phosphite fungicides for control of phytophthora root rot on azalea. Two greenhouse trials tested one or two drench applications of phosphite fungicides for control of phytophthora root rot on snapdragon and phytophthora aerial blight on petunia. Foliar and drench applications of phosphite products, including Phostrol Fungicide, provided adequate control of phytophthora root rot and aerial blight.

Based on efficacy and value considerations, the use of Phostrol Fungicide is accepted for suppression of phytophthora root rot on greenhouse-grown and outdoor bedding plants, potted plants and cut flowers, however, confirmatory data are required. The suppression claim is justified by the limited scientific evidence for Phostrol Fungicide that was provided. The extrapolation from azalea, snapdragon and petunia to greenhouse-grown and outdoor bedding plants, potted plants and cut flowers is based on similarities in pest biology, crop biology and production practices among each crop subgroup. Phostrol Fungicide may be applied as a foliar spray at 2.9-5.8 L/1000 L water or as a drench treatment at 1.2-5.6 L/1000 L water. The accepted drench rates were selected based on the tested rate range. Additional data is required to confirm the product efficacy across ornamentals at the proposed rates.

#### 5.1.1.15 Suppression of pythium blight on turf

One trial tested Phostrol Fungicide against pythium foliar blight on perennial ryegrass maintained under golf course fairway management conditions. Phostrol Fungicide was applied once at 130 and 260 mL/100 $m^2$ under severe disease pressure. As disease pressure increased (7-10 days), disease reduction decreased from 76% to 10% at 130 mL/100 $m^2$, and from 96% to 60% at 260 mL/100 $m^2$. Six supplementary trials were conducted on rough bluegrass, Bermuda grass and perennial ryegrass. In four of the six trials, phosphite fungicides suppressed pythium foliar blight up to three weeks after application. In light of these results, the use of Phostrol Fungicide is accepted for suppression of pythium blight on turf, including golf courses, sod farms, municipal, industrial and residential turf, however, confirmatory data are required. Phostrol is to be applied at 130-260 mL/100$m^2$, as the higher rate showed statistically better efficacy than the proposed rate under high disease pressure. Data on creeping bentgrass or annual bluegrass under golf course green management conditions are required to confirm product efficacy.

### 5.2 Economics

No market analysis was performed for these active ingredients.

### 5.3 Sustainability

#### 5.3.1 Survey of Alternatives

Refer to Appendix I, Table 3 for a summary of the active ingredients currently registered for the uses accepted with Phostrol Fungicide.

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

Phostrol Fungicide has shown to be compatible in tank-mix with mancozeb and chlorothalonil. Phostrol Fungicide may be used as part of an integrated pest management program.

#### 5.3.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

According to the Fungicide Resistance Action Committee, phosphite fungicides (Group 33) such as Phostrol Fungicide present a low risk of pest resistance development.

#### 5.3.4 Contribution to Risk Reduction and Sustainability

Phostrol Fungicide is a non-conventional product with a low risk of pest resistance development, which makes it a viable option for the management of certain major fungal diseases. This product is also compatible with certain conventional fungicide treatments. Its active ingredient is effective in suppressing or controlling major fungal diseases such as potato late blight and downy mildew of grape. The registration of Phostrol Fungicide would also provide growers with a much needed systemic product to manage certain plant diseases.

## 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, mono- and dibasic sodium, potassium and ammonium phosphites were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusion:

- Mono- and dibasic sodium, potassium, and ammonium phosphites are not a concern with regard to the Track 1 criteria. They are inorganic substances and are not expected to bioaccumulate in the environment.

## 6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical grade active ingredient, and formulants and contaminants in the end-use product, 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 is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8], 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:

- Phostrol 53.6% Fungicide and the end-use product Phostrol Fungicide 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 DIR2006-02[9].

---

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.*

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.

# 7.0 Summary

## 7.1 Human Health and Safety

The available information for mono- and dibasic sodium, potassium, and ammonium phosphites is adequate to identify the toxicological hazards that may result from human exposure to mono-and dibasic sodium, potassium, and ammonium phosphites. Submitted information suggests that mono- and dibasic sodium, potassium, and ammonium phosphites is of low acute toxicity irrespective of the route of exposure, minimally irritating to the eyes, mildly irritating to the skin, and not a skin sensitizer.

Although occupational exposure is expected, the precautionary statements on the product labels are sufficient to minimize any risk due to exposure of workers and bystanders.

Exposure to mono- and dibasic sodium, potassium, and ammonium phosphites from the diet or drinking water is not expected to be of concern.

## 7.2 Environmental Risk

The exposure of non-target organisms to mono- and dibasic sodium, potassium, and ammonium phosphites through the use of Phostrol Fungicide under operational conditions is not expected to cause any harmful effects to non-target terrestrial and aquatic organisms. As such, the risk to the environment is expected to be minimal.

## 7.3 Value

The following claims are accepted for Phostrol Fungicide based on the data submitted:

- suppression of downy mildew on head and stem brassicas
- suppression of phytophthora root rot on raspberries
- suppression of downy mildew on cucurbit vegetables
- control of downy mildew on grapes
- control of downy mildew on head and leaf lettuce, upland cress, endive and radicchio
- control of late blight on potatoes - foliar and post-harvest treatments
- suppression of pink rot on potatoes - foliar and in-furrow treatments
- control of pink rot on potatoes - post-harvest treatment
- control of leather rot on strawberries
- suppression of late blight on tomato crops
- suppression of phytophthora root rot on greenhouse-grown and outdoor bedding plants, potted plants and cut flowers
- suppression of pythium blight on turf

Confirmatory data are required for certain claims.

### 7.4 Unsupported Uses

Claims that were not supported, as no efficacy data or use history information was provided, are summarized in Appendix 1, Table 4.

## 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 Phostrol 53.6% Fungicide and Phostrol Fungicide, containing the technical grade active ingredient mono- and dibasic sodium, potassium and ammonium phosphites, to suppress or control several fungal diseases on a variety of vegetable and berry crops, as well as outdoor and indoor ornamentals and turf.

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

| | |
|---|---|
| λ | wavelength |
| % | percent |
| ºC | degree(s) Celsius |
| µg | microgram(s) |
| a.i. | active ingredient |
| bw | body weight |
| CAS | Chemical Abstracts Service |
| cm | centimetre(s) |
| EEC | Estimated environmental concentration |
| EIIS | Ecological Incident Information System |
| g | gram(s) |
| GRAS | generally regarded as safe |
| ha | hectare(s) |
| HDPE | high density polyethylene |
| ISP | Integrated system product |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram(s) |
| $K_{ow}$ | *n*–octanol-water partition coefficient |
| L | litre(s) |
| $LC_{50}$ | lethal concentration 50% |
| $LD_{50}$ | lethal dose 50% |
| LOC | Level of concern |
| $m^2$ | metre(s) squared |
| mg | milligram(s) |
| mL | millilitre(s) |
| MAS | maximum average score |
| MIS | maximum irritation score |
| n/a | not available |
| N/A | not applicable |
| nm | nanometre(s) |
| PAE | phosphorous acid equivalents |
| p*K*a | dissociation constant |
| PMRA | Pest Management Regulatory Agency |
| TGAI | technical grade active ingredient |
| TSMP | Toxic Substances Management Policy |
| USEPA | United States Environmental Protection Agency |
| UV | ultraviolet |

# Appendix I Tables and Figures

## Table 1 Toxicity Profile of Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphite and Its Associated End-use Product (Phostrol Fungicide)

| Study | Species, Strain And Doses | Result | Target Organ, Significant Effects, Comments | Reference |
|---|---|---|---|---|
| Acute Studies - Technical [Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites] | | | | |
| Acute oral toxicity | Sprague-Dawley rats | $LD_{50}$ > 5000 mg/kg bw<br><br>Low toxicity | Limit test performed using 24.12 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875151 |
| | Rats | $LD_{50}$ > 5000 mg/kg bw<br><br>Low toxicity | USEPA (2000) reported using 53.6 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875171 |
| Acute dermal toxicity | New Zealand White rabbits | $LD_{50}$ > 5000 mg/kg bw<br><br>Low toxicity | Limit test performed using 24.12 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875152 |
| | Rats | $LD_{50}$ > 5000 mg/kg bw<br><br>Low toxicity | USEPA (2000) reported using 53.6 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875171 |

| Study | Species, Strain And Doses | Result | Target Organ, Significant Effects, Comments | Reference |
|---|---|---|---|---|
| Acute inhalation toxicity | Sprague-Dawley rats<br><br>Whole body exposure | $LC_{50}$ > 2.06 mg/L<br><br>Low toxicity | Limit test performed using 24.12 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875154 |
| | Rats | $LC_{50}$ > 2.06 mg/L<br><br>Low toxicity | USEPA (2000) reported using 53.6 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875171 |
| Dermal irritation | New Zealand White rabbits | MAS = 0/8 (24, 48, & 72 hours after treatment)<br>MIS = 0.17/8 (one hour after treatment)<br><br>Non-irritating | Test performed using 24.12 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875156 |
| | n/a | Mildly irritating | USEPA (2000) reported the test substance was slightly irritating to the skin using 53.6 % mono- and dibasic sodium, potassium, and ammonium phosphates. The PMRA classification system considers this to be mildly irritating to the skin. | 1875171 |

| Study | Species, Strain And Doses | Result | Target Organ, Significant Effects, Comments | Reference |
|---|---|---|---|---|
| Eye irritation | New Zealand White rabbits | MAS = 0.22/110 (24, 48, & 72 hours after treatment)<br>MIS = 6.67/110 (one hour after treatment)<br><br>Minimally irritating | Test performed using 24.12 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875155 |
| | n/a | Minimally irritating | USEPA (2000) reported the test substance was irritating to the eye using 53.6 % mono- and dibasic sodium, potassium, and ammonium phosphates, but was resolved 48 hours after treatment. The PMRA classification system considers this to be minimally irritating to the eye. | 1875171 |
| Dermal sensitization | Hartley guinea pigs<br><br>(Beuhler test) | Non-sensitizer | Test performed using 24.12 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875157 |
| | n/a | Non-sensitizer | USEPA (2000) reported using 53.6 % mono- and dibasic sodium, potassium, and ammonium phosphates. | 1875171 |
| ACUTE STUDIES – END-USE PRODUCT [Phostrol Fungicide] | | | | |
| Acute oral toxicity | The end-use product, Phostrol Fungicide, is a repack of Phostrol 53.6% Fungicide. The toxicological findings are the same for both Phostrol 53.6% Fungicide and Phostrol 53.6% Fungicide.<br><br>Low toxicity | | | |

| Study | Species, Strain And Doses | Result | Target Organ, Significant Effects, Comments | Reference |
|---|---|---|---|---|
| Acute dermal toxicity | The end-use product, Phostrol Fungicide, is a repack of Phostrol 53.6% Fungicide. The toxicological findings are the same for both Phostrol 53.6% Fungicide and Phostrol 53.6% Fungicide.<br><br>Low toxicity | | | |
| Acute inhalation toxicity | The end-use product, Phostrol Fungicide, is a repack of Phostrol 53.6% Fungicide. The toxicological findings are the same for both Phostrol 53.6% Fungicide and Phostrol 53.6% Fungicide.<br><br>Low toxicity | | | |
| Dermal irritation | The end-use product, Phostrol Fungicide, is a repack of Phostrol 53.6% Fungicide. The toxicological findings are the same for both Phostrol 53.6% Fungicide and Phostrol 53.6% Fungicide.<br><br>Mildly irritating | | | |
| Eye irritation | The end-use product, Phostrol Fungicide, is a repack of Phostrol 53.6% Fungicide. The toxicological findings are the same for both Phostrol 53.6% Fungicide and Phostrol 53.6% Fungicide.<br><br>Minimally irritating | | | |
| Dermal sensitization | The end-use product, Phostrol Fungicide, is a repack of Phostrol 53.6% Fungicide. The toxicological findings are the same for both Phostrol 53.6% Fungicide and Phostrol 53.6% Fungicide.<br><br>Non-sensitizer | | | |

**Table 2 Short-term Toxicity, Prenatal Development Toxicity, and Genotoxicity of Technical Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites**

| Study | Species, Strain And Doses | Result | Target Organ, Significant Effects, Comments | Reference |
|---|---|---|---|---|
| **Short-Term Toxicity** | | | | |
| 90-day dietary | Sufficient information was available, as well as a history of use in agriculture, to suggest that treatment-related effects would not be anticipated. | | | |
| **Reproduction And Developmental Toxicity** | | | | |
| Prenatal developmental toxicity | Sufficient information was available, as well as a history of use in agriculture, to suggest that treatment-related effects would not be anticipated. | | | |
| **Genotoxicity** | | | | |
| **Study** | **Species And Strain Or Cell Type** | **Results** | | **Reference** |
| Gene mutations in bacteria | *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537, and TA 1538; *E. coli*; *Saccharomyces cereviscae* | Negative<br><br>Aluminum tris(ethyl phosphite), Aliette, was tested and based on its molecular structure, as well as any structural analogues, it appears unlikely that exposure to mono- and dibasic sodium, potassium, and ammonium phosphites would result in bacterial mutations. | | 1898193 |
| Gene mutations in mammalian cells *in vitro* | Sufficient information was available, as well as a history of use in agriculture, to suggest that treatment-related effects would not be anticipated. | | | |

**Table 3 Summary of Fungicide Alternatives for the Uses Supported with Phostrol Fungicide**

| Crop | Pests | Active Ingredient and Resistance Management Group |
|---|---|---|
| Head and stem brassicas | Downy mildew | boscalid (7) + pyraclostrobin (11)<br>fenamidone (11)<br>mandipropamid (40)<br>fluopicolide (43)<br>*Bacillus subtilis* (44) |
| Raspberries | Phytophthora root rot | metalaxyl (4)<br>fosetyl-al (33)<br>chloropicrin (F) |
| Cucurbit vegetables | Downy mildew | fenamidone (11)<br>pyraclostrobin (11)<br>cyazofamid (21)<br>mandipropamid (40)<br>*Bacillus subtilis* (44)<br>chlorothalonil (M5)<br>propamocarb hydrochloride (U) + chlorothalonil (M5) |
| Grapes | | metalaxyl (4) + mancozeb (M3)<br>boscalid (7) + pyraclostrobin (11)<br>kresoxim-methyl (11)<br>zoxamide (22)<br>zoxamide (22) + mancozeb (M3)<br>mandipropamid (40)<br>fluopicolide (43)<br>copper (M1)<br>mancozeb (M3)<br>metiram (M3)<br>captan (M4)<br>folpet (M4) |
| Head and leaf lettuce | Downy mildew | metalaxyl (4) + mancozeb (M3)<br>fosetyl-al (33)<br>mandipropamid (40)<br>fluopicolide (43)<br>*Bacillus subtilis* (44) |

| Crop | Pests | Active Ingredient and Resistance Management Group |
|---|---|---|
| Upland cress, endive, radicchio | Downy mildew | N/A |
| Potatoes | Late blight | metalaxyl (4) + mancozeb (M3)<br>metalaxyl (4) + chlorothalonil (M5)<br>azoxystrobin (11)<br>famoxadone (11) + cymoxanil (27)<br>pyraclostrobin (11)<br>cyazofamid (21)<br>zoxamide (22)<br>zoxamide (22) + mancozeb (M3)<br>fluazinam (29)<br>mono- and di-potassium salts of phosphorous acid (33)<br>dimethomorph (40)<br>mandipropamid (40)<br>fluopicolide (43)<br>copper (M1)<br>mancozeb (M3)<br>mancozeb (M3) + chlorothalonil (M5)<br>metiram (M3)<br>captan (M4)<br>chlorothalonil (M5)<br>propamocarb hydrochloride (U) + chlorothalonil (M5) |
| Potatoes | Pink rot | metalaxyl (4)<br>metalaxyl (4) + mancozeb (M3)<br>metalaxyl (4) + chlorothalonil (M5)<br>azoxystrobin (11)<br>mono- and di-potassium salts of phosphorous acid (33)<br>mancozeb (M3) + chlorothalonil (M5) |
| Strawberries | Leather rot | N/A |

| Crop | Pests | Active Ingredient and Resistance Management Group |
|---|---|---|
| Tomatoes | Late blight | famoxadone (11) + cymoxanil (27) |
| | | pyraclostrobin (11)<br>mandipropamid (40)<br>fluopicolide (43)<br>copper (M1)<br>mancozeb (M3)<br>metiram (M3)<br>ziram (M3)<br>captan (M4)<br>chlorothalonil (M5) |
| Greenhouse-grown and outdoor<br>bedding plants, potted plants and<br>cut flowers* | Phytophthora root rot | etridiazole (14)<br>fosetyl-al (33)<br>fluopicolide (43)<br>*Bacillus subtilis* (44)<br>chlorothalonil (M5)<br>*Streptomyces* sp. (NC)<br>propamocarb hydrochloride (U) |
| Turf | Pythium blight | propiconazole (3) + azoxystrobin (11)<br>azoxystrobin (11)<br>pyraclostrobin (11)<br>propamocarb hydrochloride (U)<br>fosetyl-al (33) |

*The listed fungicides are registered for use on specific ornamental plants

**Table 4 Phostrol Fungicide Use (label) Claims Proposed by Applicant and Whether Acceptable or Unsupported**

| Proposed claim | Supported / Unsupported |
|---|---|
| **Asparagus**: control of spear slime and crown rot (*Phytophthora megasperma*) with one foliar application at 2.9-5.8 L/ha. | Not supported. No efficacy data was provided. |
| **Bushberries**: control of phytophthora root rot (*Phytophthora* spp.) with a maximum of 4 foliar applications at 2.9-5.8 L/ha on a 14-21 day schedule. | Not supported. No efficacy data was provided. |

| Proposed claim | Supported / Unsupported |
|---|---|
| **Head and stem brassica subgroup**: control of downy mildew (*Peronospora parasitica*) with a maximum of 4 foliar applications at 2.9-5.8 L/ha on a 7-21 day schedule | Supported for suppression, however, confirmatory data are required. |
| **Caneberries**: control of root rot (*Phytophthora* spp.) with a maximum of 4 foliar applications at 5.2 L/ha. Phostrol is to be sprayed at spring or fall under specific application instructions. | Supported for suppression on raspberries, however, confirmatory data are required. |
| **Cucurbit vegetables**: control of downy mildew (*Pseudoperonospora cubensis*) with a maximum of 7 foliar applications at 5.2 L/ha on a 7-14 day schedule. | Supported for suppression, however, confirmatory data are required. |
| **Small fruit vine climbing subgroup, except fuzzy kiwifruit**: control of downy mildew (*Plasmopara viticola*) with a maximum of 4 foliar applications at 2.9-5.8 L/ha on a 7-day schedule. | Supported on grapes. |
| **Leafy greens**: control of downy mildew (*Bremia lactucae*, *Peronospora farinosa*, *P. jaapina*, *P. umbelliferarum*) with a maximum of 7 foliar applications at 2.9-5.8 L/ha on a 7-21 day schedule. | Supported for control of downy mildew (*Bremia lactucae*) on lettuce, upland cress, endive and radicchio. Application intervals: 7-14 days. |
| **Bulb vegetables**: control of downy mildew (*Peronospara destructor*) with a maximum of 7 foliar applications at 2.9-4.3 L/ha on a 7-14 day schedule. | Not supported. No efficacy data was provided. |
| **Tuberous and corm vegetables**: suppression of pink rot (*Phytophthora erythroseptica*) with one in-furrow application at 4.5-11.6 L/ha. | Supported for suppression on potatoes at 5.8-11.6 L/ha, however, confirmatory data are required. |
| **Tuberous and corm vegetables**: control of late blight (*Phytophthora infestans*) and pink rot (*Phytophthora erythroseptica*) with a maximum of 7 foliar applications at 2.9-11.6 L/ha on a 4-14 day schedule. | Supported on potatoes for control of late blight (*Phytophthora infestans*) at 2.9-11.6 L/ha. Application intervals: 7-14 days |
| | Supported on potatoes for suppression of pink rot (*Phytophthora erythroseptica*) at 5.8-11.6 L/ha. Application intervals: 7-14 days |
| **Tuberous and corm vegetables**: control of late blight (*Phytophthora infestans*) and pink rot (*Phytophthora erythroseptica*) with one post-harvest application at 0.42 L Phostrol in 2 L water to 1 tonne tubers. | Supported on potatoes. |
| **Tuberous and corm vegetables**: aerial applications | Supported on potatoes, however, confirmatory data are required. |
| **Low growing berries**: control of leather rot (*Phytophthora cactorum*) with a maximum of 4 foliar applications at 2.9-5.8 L/ha. | Supported on strawberries at 4.1 L/ha, however, confirmatory data are required. |

| Proposed claim | Supported / Unsupported |
|---|---|
| **Cranberries**: control of root rot (*Phytophthora* spp.) with a maximum of 4 foliar applications at 5.8-7.0 L/ha on a 14-30 day schedule. | Not supported. No efficacy data was provided. |
| **Tomato subgroup**: suppression of late blight (*Phytophthora infestans*) with a maximum of 4 foliar applications at 2.9-5.8 L/ha on a 7-14 day schedule. | Supported as proposed. |
| **Tomato subgroup**: control of root rot (*Pythium* spp.) with a maximum of 4 foliar applications at 2.9-5.8 L/ha on a 14-30 day schedule. | Not supported. No efficacy data was provided. |
| **Pepper/eggplant subgroup** (Crop Subgroup 8-09B): control of *Phytophthora* spp. and *Pythium* spp. with a maximum of 4 foliar applications at 2.3-4.6 L/ha on a 14-21 day schedule. | Not supported. No efficacy data was provided. |
| **Outdoor ornamentals (field-grown deciduous and coniferous trees and shrubs; container-grown deciduous and coniferous woody ornamentals, shrubs and herbaceous perennials)**: control of root rot (*Phytophthora* spp.) with a maximum of 6 foliar applications at 2.9-5.8 L/1000 L water. Do not apply more than once every 30 days. | Supported for suppression on greenhouse-grown and outdoor bedding plants, potted plants and cut flowers, however, confirmatory data are required. |
| **Outdoor ornamentals (field-grown deciduous and coniferous trees and shrubs; container-grown deciduous and coniferous woody ornamentals, shrubs and herbaceous perennials)**: control of root rot (*Phytophthora* spp.) with a maximum of 6 drench applications at 0.9-1.8 L/1000 L water. Apply 10 L of solution per $m^2$. Do not apply more than once every 30 days. | Supported for suppression on greenhouse-grown and outdoor bedding plants, potted plants and cut flowers at 1.2-5.6 L/1000 L water, however, confirmatory data are required. |
| **Indoor greenhouse ornamentals (bedding plants, potted plants, cut flowers)**: control of root rot (*Pythium* spp.) with a maximum of 6 foliar applications at 1.5-4.6 L/1000 L water on a 14-day schedule. | Not supported. No efficacy data was provided. |
| **Turf (golf course, sod farms, municipal, industrial and residential turf)**: control of root rot and blight (*Pythium* spp.) with a maximum of 4 foliar applications at 130 mL/100 $m^2$ on a 14-day schedule. | Supported for suppression of pythium blight (*P. aphanidermatum*) at 130-260 mL/100 $m^2$, however, confirmatory data are required. |

# References

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

### 1.0 Chemistry

PMRA Document Number: 1875135
Reference: 2010, Waiver for the Request of Daco 2 Chemistry Data for Phostrol Fungicide, DACO:
2.13.1,2.13.2,2.13.3,2.14.11,2.14.12,2.14.13,2.14.5,2.14.8,2.15,2.4,2.5 CBI

PMRA Document Number: 1875136
Reference: 2010, Product Identification for DACO 3.1.1 to 3.1.4 for Phostrol Fungicide, DACO: 3.1.1, 3.1.2, 3.1.3, 3.1.4 CBI

PMRA Document Number: 1875138
Reference: 2002, Description of Materials Used to Produce the Product and Description of the Production Process, DACO: 3.2.1, 3.2.2 CBI

PMRA Document Number: 1875139
Reference: 2010, DACO 3.0 Product Chemistry: DACO 3.2.2 Comparison of Nufarm and Proposed Engage Agro Formulations, DACO: 3.2.2 CBI

PMRA Document Number: 1875140
Reference: 2000, Product Identity and Composition, Description of Materials Used to Produce the Product, Description of the Production Process, and Discussion of Formation of Impurities, DACO: 3.2.3, 3.5.2 CBI

PMRA Document Number: 1875141
Reference: 2000, Composition, Certified Limits and Enforcement Analytical Methods, DACO: 3.3.1, 3.4.1 CBI

PMRA Document Number: 1875144
Reference: 2000, Final Report for Preliminary Analysis of Phostrol, DACO: 3.4.1 CBI

PMRA Document Number: 1875145
Reference: 1999, Product Properties: Color, Physical State, Odour, Chemical Incompatibility, Storage Stability, Corrosion Characteristics, pH, Viscosity, Melting Point, Density, Dissociation Constant, Water Solubility, and Vapour Pressure, DACO: 3.5.1,3.5.10,3.5.11,3.5

PMRA Document Number: 1875146
Reference: 1999, Final Report: Physical and Chemical Characteristics of Agtrol Neutralized Phosphite, DACO: 3.5.1, 3.5.10, 3.5.14, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.9 CBI

PMRA Document Number: 1875147
Reference: 2010, Formulation Type and Container Material and Description for Phostrol Fungicide, DACO: 3.5.4, 3.5.5 CBI

PMRA Document Number: 1875148
Reference: 2009, Rationale to Support the Registration of Phostrol Fungicide as an Integrated System Product under the Pest Control Products Act., DACO: 3.7 CBI

PMRA Document Number: 1942196
Reference: 2010, Product Identification for DACO 3.1.1 to 3.1.4 for Phostrol Fungicide, DACO: 3.1.1, 3.1.2, 3.1.3, 3.1.4 CBI.

PMRA Document Number: 1898202
Reference: 2010, Product Identification for DACO 2.1 to 2.3.1 and 2.7 for Phostrol 53.6% Fungicide, DACO: 2.1, 2.2, 2.3, 2.3.1, 2.7 CBI

PMRA Document Number: 1942205
Reference: 2010, Product Identification for DACO 2.1 to 2.3.1 and 2.7 for Phostrol 53.6% Fungicide, DACO: 2.1, 2.2, 2.3, 2.3.1, 2.7 CBI

## 2.0 Human and Animal Health

PMRA Document Number: 1875151
Reference: 1999, Acute Oral Toxicity Limit Test, DACO: 4.2.1

PMRA Document Number: 1875152
Reference: 1999, Acute Dermal Toxicity Limit Test, DACO: 4.2.2

PMRA Document Number: 1875154
Reference: 1999, Acute Inhalation Toxicity Limit Test, DACO: 4.2.3

PMRA Document Number: 1875155
Reference: 1999, Primary Eye Irritation, DACO: 4.2.4

PMRA Document Number: 1875156
Reference: 1999, Primary Skin Irritation, DACO: 4.2.5

PMRA Document Number: 1875157
Reference: 1999, Dermal Sensitization Test - Buehler Method, DACO: 4.2.6

PMRA Document Number: 1875158
Reference: 2010, Use Description and Scenario (Mixer/Loader/Applicator and Postapplication) for Phostrol Fungicide, DACO: 5.2

PMRA Document Number: 1875159
Reference: 2010, DACO 6.1: Summary and Rationale: Metabolism, Pharmacokinetics, DACO: 6.1

PMRA Document Number: 1875160
Reference: 2010, DACO Part 7.1: Summary and Rationale - Food Residue Exposure Assessment, DACO: 7.1

PMRA Document Number: 1875167
Reference: 1999, Notice of Filing a Pesticide Petition to Establish a Tolerance for Certain Pesticide Chemicals in or on Food, DACO: 12.5.3,M12.5.4

PMRA Document Number: 1875168
Reference: 1998, Mono- and Di-potassium Salts of Phosphorous Acid (076416) Fact Sheet, DACO: 12.5.4,12.5.5,12.5.6,12.5.7,12.5.9

PMRA Document Number: 1875169
Reference: 2006, Phosphorous Acid; Exemption from the Requirement of a Tolerance, DACO: M12.5.4,M12.5.7

PMRA Document Number: 1875170
Reference: 2006, Phosphorous Acid; Proposed Amendment to Exemption of Tolerance, DACO: M12.5.4,M12.5.7

PMRA Document Number: 1875171
Reference: 2000, Phosphorous Acid; Exemption from the Requirement of a Tolerance, DACO: M12.5.4,M12.5.7

PMRA Document Number: 1875172
Reference: 2000, Phosphorous Acid and its Ammonium, Sodium and Potassium Salts (076002) Mono- and di-potassium salts of Phosphorus Acid (076416) Fact Sheet, DACO: M12.5.4,M12.5.9

PMRA Document Number: 1875173
Reference: 2002, New York State Department of Environmental Conservation: Registration of Phostrol Agricultural Fungicide Letter, DACO: M12.5.4,M12.5.9

PMRA Document Number: 1875174
Reference: Agronomy Series Timely Information: Agriculture and Natural Resources; Phosphites as Fertilizer, DACO: M12.5.10

PMRA Document Number: 1875175
Reference: 2010, Comprehensive Summary for Phostrol Fungicide, DACO: 12.7

PMRA Document Number: 1898193
Reference: 2010, Waiver for the Request of Short-Term 90-Day Oral (4.3.1), Developmental Toxicity (4.5.2) and Genotoxicity Studies (4.5.4 & 4.5.5), DACO: 4.1,4.3.1,4.5.2,4.5.4,4.5.5

## 3.0 Environment

PMRA Document Number: 1875161
Reference: 2010, DACO Part 9.1: Summary and Rationale - Ecotoxicology, DACO: 9.1,9.2.4.1,9.3.2,9.5.2.1,9.6.2.1,9.6.2.4,9.8.4

PMRA Document Number: 1875168
Reference: 1998, Mono- and di-potassium Salts of Phosphorous Acid (076416) Fact Sheet, DACO: 12.5.4,12.5.5,12.5.6,12.5.7,12.5.9

PMRA Document Number: 1875173
Reference: 2002, New York State Department of Environmental Conservation: Registration of Phostrol Agricultural Fungicide Letter, DACO: 12.5.4, 12.5.9

PMRA Document Number: 1875174
Reference: Agronomy Series Timely Information: Agriculture and Natural Resources; Phosphites as Fertilizer, DACO: 12.5.10

PMRA Document Number: 1875175
Reference: 2010, Comprehensive Summary for Phostrol Fungicide, DACO: 12.7

## 4.0 Value

PMRA Document Number: 1875162
Reference: 2010, Value Summary for Phostrol Fungicide, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.2, 10.2.3.3, 10.2.3.4, 10.3.1, 10.3.2, 10.3.3, 10.4, 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.6

PMRA Document Number: 1875163
Reference: 2010, Value Summary - Appendix 2, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.2, 10.2.3.3, 10.2.3.4, 10.3.1, 10.3.2, 10.3.3, 10.4, 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.6

PMRA Document Number: 1875164
Reference: 2010, Value Summary - Appendix 3, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3.1, 10.2.3.2, 10.2.3.3, 10.2.3.4, 10.3.1, 10.3.2, 10.3.3, 10.4, 10.5.1, 10.5.2, 10.5.3, 10.5.4, 10.6

PMRA Document Number: 1875165
Reference: Efficacy and Crop Tolerance Summary Table - Phostrol Fungicide, DACO: 10.2.3.1, 10.3.1

PMRA Document Number: 1875166
Reference:Efficacy and Crop Tolerance Summary Table - Phosphites, DACO: 10.2.3.1, 10.3.1

PMRA Document Number: 2011498
Reference: 2011, Phostrol Fungicide Deficiency Response, DACO: 10.2.3.1

PMRA Document Number: 2011499
Reference: 2005, Appendix 1, DACO: 10.2.3.3

PMRA Document Number: 2011501
Reference: 2011, Appendix 2, DACO: 10.2.3.3

PMRA Document Number: 2011502
Reference: 2010, Appendix 3, DACO: 10.2.3.3

PMRA Document Number: 2011503
Reference: Appendix 4, DACO: 10.2.3.3

PMRA Document Number: 2011504
Reference: 2011, Appendix 5, DACO: 10.2.3.3

PMRA Document Number: 2011505
Reference: 2010, Appendix 6, DACO: 10.2.3.3

PMRA Document Number: 2011506
Reference: 2011, Appendix 7, DACO: 10.2.3.3

## B. Additional Information Considered

### i) Published Information

### 1.0 Environment

PMRA Document Number: 2149365
Reference: Lee, T.-M., Tsai, P.-F., Shyu, Y.-T., and Sheu, F. 2005. The effects of phosphite on phosphate starvation responses of *Ulva Lactuca* (Ulvales, Chlorophyta). J. Phycol. 41: 975-982.

PMRA Document Number: 2149381
Reference: Varadarajan, D.K., Karthikeyan, A.S., Durzo Matilda, P., and Raghothama, K.G. 2002. Phosphite, an analog of phosphate, suppresses the coordinated expression of genes under phosphate starvation. Plant Physiol. 129: 1232-1240.

PMRA Document Number: 2152658
Reference: Ratjen, A.M., and Gerendas, J. 2009. A critical assessment of the suitability of phosphite as a source of phosphorus. J. Plant Nutr. Soil Sci. 172: 821-828.

PMRA Document Number: 2152959
Reference: Martinez, A., Osburne, M.O., Sharma, A.K., DeLong, E.F., and Chrisholm, S.W. 2011. Phosphite utilization by the marine picocyanobacterium Prochlorococcus MIT9301. Environ. Microbiol. 1462-2920.