Evaluation Report ERC2010-09

Mono- and Di-Potassium Salts of Phosphorous Acid

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Overview

Registration Decision for Mono- and Di-Potassium Salts of Phosphorous Acid

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for the sale and use of Mono- and Di-Potassium Salts of Phosphorous Acid and Confine containing the technical grade active ingredient mono- and di-potassium salts of phosphorous acid for suppression of late blight and pink rot on harvested potato tubers.

Current scientific data from the applicant were evaluated to determine if, under the proposed conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This report summarizes the information that was evaluated and provides the results of the evaluation as well as the reasons for the registration decision, with an outline of the additional scientific information required from the applicant. It also describes the conditions of registration that the applicant must meet to ensure that the health and environmental risks as well as the value of these pest control products are acceptable for their intended use.

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of Mono- and Di-Potassium Salts of Phosphorous Acid and Confine.

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.

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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".

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). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, and on 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.

What Is Mono- and Di-Potassium Salts of Phosphorous Acid?

Mono- and di-potassium salts of phosphorous acid, or phosphorous acid, is a fungicide active ingredient belonging to Group 33 of the Fungicide Resistance Action Committee and is classified as a phosphonate. The mode of action of phosphorous acid is both direct and indirect. Mono- and di-potassium salts of phosphorous acid is the active ingredient in the fungicide Confine, which is registered for suppression of late blight and pink rot on harvested potato tubers.

Health Considerations

Can Approved Uses of Mono- and Di-Potassium Salts of Phosphorous Acid Affect Human Health?

Mono- and Di-Potassium Salts of Phosphorous Acid is unlikely to affect human health when used according to label directions.

Exposure to mono- and di-potassium salts of phosphorous acid 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 di-potassium salts of phosphorous acid is of low toxicity by the oral, dermal and inhalation routes, and only minimally irritating to the eyes. The precautionary label statement indicating that contact with eyes must be avoided, and the personal protective equipment statement that applicators and other handlers must wear protective eyewear are effective mitigative measures to reduce the risk associated with the use of this chemical.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Mono- and di-potassium salts of phosphorous acid is of low acute toxicity by the oral, dermal and inhalation routes. It is minimally irritating to the eyes, non-irritating to the skin and is not a skin sensitizer. The available information suggests that it is unlikely to have any short-term or prenatal developmental effects, as well as any significant genotoxic effects.

Dietary risk to humans is considered negligible based on the intended use, method of application, low application rate, 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 proposed use of mono- and di-potassium salts of phosphorous acid in Canada on stored potatoes will not pose a risk to any segment of the population, including infants, children, adults and seniors, when potatoes 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 phosphoric 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.

This end-use product will be used in a contained treatment area and will not be applied to water. No risk due to exposure from drinking water is anticipated.

Occupational Risks From Handling Mono- and Di-Potassium Salts of Phosphorous Acid

Occupational risks are not of concern when mono- and di-potassium salts of phosphorous acid is used according to label directions, which include protective measures.

Occupational exposure to mono- and di-potassium salts of phosphorous acid is expected to be minimal as application is done by automated enclosed spray chamber, which sprays newly-harvested potatoes when they pass along a conveyor belt towards storage bins. Precautionary statements on the label (for example, wearing of personal protective equipment and clothing) are considered adequate to protect individuals from any unnecessary risk due to exposure. Given the method of application and low toxicity of the end-use product, bystander exposure risk is anticipated to be negligible.

Environmental Considerations

What Happens When Mono- and Di-Potassium Salts of Phosphorous Acid Is Introduced Into the Environment?

Mono- and di-potassium salts of phosphorous acid is used in the formulation of Confine fungicide for the suppression of late blight and pink rot storage infection in russet-skinned potatoes or potatoes intended for processing. Since the end-use product will be used indoors on post-harvest potatoes, the risk to non-target organisms is considered to be negligible, when used according to the label. Because of the use pattern, Confine is unlikely to be introduced to the environment.

Value Considerations

What Is the Value of Confine Fungicide?

Confine fungicide is to be used for post-harvest suppression of late blight and pink rot in potato tubers. Currently, there are no other products registered for this use.

Measures to Minimize Risk

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

The key risk-reduction measures on the label of Confine to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

Human Health

Because mono- and di-potassium salts of phosphorous acid is used for formulating a commercial product, the statement on the technical label: “prevent access by unauthorized personnel” in the precaution section of the technical label will help mitigate the inappropriate use of the product, and help avoid accidental 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.

What Additional Scientific Information is Being Requested?

Although the risks and value have been found acceptable when all risk reduction measures are followed, the registrant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The registrant must submit the following information within the time frames indicated.

Chemistry

The following studies are required to complete the chemistry database for this product:

- Storage stability data for the end-use product representing at least one year of storage at ambient conditions

- Corrosion data for the end-use product representing at least one year of storage at ambient conditions

Value

- The longest interval between treatment with Confine fungicide and disease assessment in the trials provided for this application was 77 days. This is not sufficient to fully support a claim for suppression of late blight and pink rot of stored potatoes, since potatoes may be stored for as long as 10 months. A claim for suppression implies a consistent lower level of control compared to industry expectations that lasts for the duration of the storage period. At least two additional trials demonstrating the efficacy of Confine fungicide for up to 8 months are required.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted[3], the PMRA will publish a consultation document when there is a proposed decision on applications to convert the conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

The test data cited in this *Evaluation Report* (i.e., the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

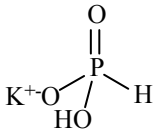
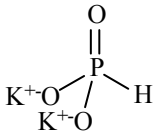
[3] As per subsection 28(1) of the *Pest Control Products Act.*

Science Evaluation

Mono- and Di-Potassium Salts of Phosphorous Acid

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Potassium phosphite	
Function	Fungicide	
Chemical name		
1. International Union of Pure and Applied Chemistry (IUPAC)	Monopotassium phosphonate and Dipotassium phosphonate	
2. Chemical Abstracts Service (CAS)	Phosphonic acid, monopotassium salt and Phosphonic acid, dipotassium salt	
CAS number	Mono-potassium phosphite	13977-65-6
	Di-potassium phosphite	13492-26-7
Molecular formula	KH_2PO_3 and K_2HPO_3	
Molecular weight	120.09 and 158.19	
Structural formula		
	13977-65-6	13492-26-7
Purity of the active ingredient	45.8%	

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

Technical Product—Mono- and di-potassium salts of phosphorous acid

Property	Result
Colour and physical state	Colourless liquid
Odour	Odourless
Melting range	Not applicable

Property	Result
Boiling point	105.5°C
Specific gravity at 20°C	1.358
Henry's law constant at 20°C	Not applicable
Ultraviolet (UV)-visible spectrum	λ_{max} = 257 nm, no absorption >350 nm
Solubility in water at 20°C	miscible
Solubility in organic solvents at 20°C (g/100 mL)	Insoluble in organic solvents
n-Octanol-water partition coefficient (K_{ow})	Not applicable (insoluble in n-octanol)
Dissociation constant (pK_a)	pK_{a1} = 1.37, pK_{a2} = 6.57
Stability (temperature, metal)	Unstable to metal and metal irons (iron powder, ferric chloride, lead shot, lead nitrate)

End-Use Product—Confine

Property	Result
Colour	Colourless
Odour	Odourless
Physical state	Liquid
Formulation type	Liquid
Guarantee	45.8%
Container material and description	2 × 2.5 gal PVC containers
Specific gravity at 20°C	1.358
pH of 1% dispersion in water	5.5
Oxidizing or reducing action	Neither an oxidant nor a reductant
Storage stability	Not available
Corrosion characteristics	Not available
Explodability	Not explosive

1.3 Directions for Use

For the post-harvest suppression of late blight (*Phytophthora infestans*) and pink rot (*P. erythroseptica*) on potatoes, dilute Confine at 1:4.3 ratio with water. Apply 2 L of the mixture as a spray to 1000 kg of potatoes. Ensure complete and even coverage. Use only on russet-skinned varieties, or potatoes intended for processing.

1.4 Mode of Action

The mode of action of phosphorous acid is both direct and indirect. It inhibits fungal growth in oomycetes, a group of fungal-like organisms. In addition, there is also evidence that it stimulates the plant's natural defense response against pathogen attack. A major factor in the ability of phosphorous acid to control oomycetes is its chemical stability within the plant. Phosphorous acid does not convert to phosphate and is not easily metabolized.

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 mono- and di-potassium salts of phosphorous acid have been assessed to be acceptable.

2.2 Method for Formulation Analysis

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

2.3 Methods for Residue Analysis

Not required for this application.

3.0 Impact on Human and Animal Health

3.1 Toxicological Summary

The PMRA has conducted a detailed review of the submitted data for mono- and di-potassium phosphorous acid. 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 qualitatively assess the toxicological hazards of this pest control product.

Submitted information for the technical grade active ingredient, mono-and di-potassium salts of phosphorous acid, and the end-use product, Confine (45.8 % w/w mono- and di-potassium salts of phosphorous acid), suggests that the active ingredient is of low acute toxicity by the oral, dermal, and inhalation routes of exposure. Mono- and di-potassium salts of phosphorous acid is non-irritating to the skin, minimally irritating to the eyes, and is not a skin sensitizer.

Information on short-term toxicity, developmental toxicity (prenatal), and genotoxicity were not available for mono- and di-potassium salts of phosphorous acid at the time of evaluation. However, based on the general toxicological information together with a long history of safe use as a commodity chemical and its use as a pesticide in Australia and the United States, it appears unlikely that treatment-related effects will result from exposure to mono- and di-potassium salts of phosphorous acid.

The mutagenicity of mono- and di-potassium salts of phosphorous acid was assessed with the reverse gene mutation assay in bacteria (Ames assay). *Salmonella typhimurium* strains TA 97, TA 98, TA 100, TA 1535 and TA 1537 and *E. Coli* WP2uvrA were exposed to Agri-Fos 400 (313, 625, 1250, 2500, and 5000 μg/plate) with and without metabolic activation (S9). The findings were negative in that there was no evidence of a treatment-related response over background.

3.2 Determination of Acceptable Daily Intake

An acceptable daily intake is not required because of the anticipated negligible risk to human health from the ingestion of potatoes treated with Confine, due to the low acute toxicity of mono- and di-potassium salts of phosphorous acid and an established history of safe use in other parts of the world. Potassium salts of phosphorous acid are widely used globally in the production of fertilizers, insecticides, fungicides, antiviral medicines, and some herbicides. In the United States, phosphorous acid has been designated Generally Regarded As Safe (GRAS) and the potassium salts of phosphoric 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 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.

3.3 Determination of Acute Reference Dose (ARfD)

An acute reference dose is not required due to the low acute toxicity of mono- and di-potassium salts of phosphorous acid. The available literature suggests that there is no significant treatment-related effect to indicate a concern for acute dietary risk assessment.

3.4 Occupational and Bystander Risk Assessment

3.4.1 Toxicological Endpoints

The end-use product, Confine, is of low acute toxicity by the oral, dermal and inhalation routes. It is minimally irritating to the eyes, non-irritating to the skin and is not a skin sensitizer. The available information suggests that the end-use product is unlikely to have any short-term or prenatal developmental effects, as well as any significant genotoxic effects. A toxicologically significant endpoint appears to be a local, rather than a systemic effect. Transient ocular irritation appears to be the only treatment-related effect. Occupational exposure to Confine is expected to be minimal, as application is done by automated enclosed spray chamber.

3.4.2 Dermal Absorption

Dermal exposure is expected to be minimal due to the use pattern of the product and the method of application. Since the available literature suggests a negligible dermal absorption of mono- and di-potassium salts of phosphorous acid and since adequate hygiene statements are on the product label, a dermal absorption study was not considered necessary to complete the health hazard assessment of mono- and di-potassium salts of phosphorous acid.

3.4.3 Mixer, Loader and Applicator Exposure and Risk Assessment

Significant exposure to the mixer, loader, and applicator, as well as those responsible for clean up and maintenance activities, is not anticipated. Confine is used to suppress fungal diseases while potatoes are in storage. Application is done mainly during the harvesting and storage period in the autumn. The product is to be applied only once, as a low volume spray to harvested potatoes as they are being automatically loaded into bulk storage bins. An enclosed spray chamber mounted on the conveyor sprays newly-harvested potatoes as they pass along a conveyor belt towards storage bins.

3.4.4 Bystander Exposure and Risk Assessment

Given the method of application, which minimizes exposure and low toxicity of the end-use product, the risk to bystanders is anticipated to be negligible.

3.4.5 Post Application Exposure

After spraying, potatoes remain in storage for 2-10 months before handling further. Residues of toxicological concern are not expected. Therefore, post-application exposure is not expected to be of concern.

3.4.6 Food Residue Exposure Assessment

The PMRA has not established an acceptable daily intake. It is anticipated that the use of mono- and di-potassium salts of phosphorous acid in Canada on stored potatoes will not pose a risk to any segment of the population, including infants, children, adults and seniors, when potatoes are subjected to the normal process of washing, peeling and cooking for human consumption.

4.0 Impact on the Environment

Because mono- and di-potassium salts of phosphorous acid and the end-use product Confine fungicide are used post-harvest indoors, the risk to non-target organisms is considered to be negligible when used according to the label.

5.0 Value

5.1 Effectiveness Against Pests

Five trials on post-harvest treatment of potatoes were provided to support the claims. Two trials were conducted in Canada (Prince Edward Island and Alberta) in 2006-2007. The other three trials were conducted in Idaho from 2005-2006. All trials tested rates very close to the proposed dilution rate of 1:4.3 (1:5; 1:6 and 1:10 dilution). The results show that one application of Phostrol, containing the same active ingredient as Confine, at a 1:6 dilution rate reduced late blight incidence by 96% (trial 1). Late blight severity was reduced by 97-100% (trials 1, 3, 4, and 5) on potato tubers treated with either Phostrol or Confine at a 1:10 or a 1:5 dilution rate. No significant differences in disease control were observed when ratios of 1:4 or 1:6-1:20 were used. However, higher ratios such as 1:40 -1:75 decreased disease control correspondingly.

Pink rot severity decreased by 96-98% compared to untreated controls while incidence decreased by 92- 100%. The sensitivity of metalaxyl-M–sensitive or metalaxyl-M-resistant *P. erythroseptica* to phosphorous acid fungicide did not significantly differ. Both populations of *P. erythroseptica* were controlled by Confine or Phostrol from 84-100% (metalaxyl-M-resistant) and 95-100% (metalaxyl-M-sensitive).

Phosphorous acid did not affect tuber processing quality. Glucose and sucrose content did not significantly differ between Phostrol-treated potatoes and the untreated controls. Mean fry colour ratings were also the same for both sets of tubers.

5.1.1 Acceptable Efficacy Claims

The claim for suppression of pink rot and late blight on storage potatoes, when applied once as a post-harvest treatment at the dilution rate of 1:4.3, is supported. Additional trials are required to demonstrate the efficacy of Confine fungicide to reflect the length of time that potatoes may be stored.

5.2 Phytotoxicity to Host Plants

The registrant indicated that the active ingredient contained in Confine may affect light-skinned potatoes (PMRA 1510746). Therefore, only russet-skinned and processing potatoes have been included on the label.

5.3 Economics

No market analysis was provided for this application.

5.4 Sustainability

5.4.1 Survey of Alternatives

Currently, there are no products registered for the control/suppression of late blight or pink rot on stored potatoes in Canada.

5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

The use of Confine fungicide on stored potatoes will contribute to the management of potato late blight and pink rot of potatoes.

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

There are some reports of *Phytopthora* spp. resistant to phosphonates (PMRA# 1510748). It is, therefore, very important to take the appropriate steps to prevent rapid development of resistance in *P. erythrospetica* and *P. infestans*. At this time, there are no resistance management concerns with the proposed use since Confine will be applied only once per season. However, resistance management must be taken into consideration when assessing future potential amendments to the use pattern of phosphorous acid. Label amendments will include the addition of the resistance management wording as required by DIR1999-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, mono- and di-potassium salts of phosphorous acid was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of mono- and di-potassium salts of phosphorous acid were also considered, including transformation products formed in the environment, and contaminants and formulants in the technical product and the end-use product. Mono- and di-potassium salts of phosphorous acid and its transformation products were evaluated against the following Track 1 criteria: persistence in soil ≥182 days; persistence in water ≥182 days; persistence in sediment ≥365 days; persistence in air ≥2 days; bioaccumulation log K_{ow} ≥5 or BCF ≥5000 (or BAF ≥5000). In order for mono- and di-potassium salts of phosphorous acid or its transformation products to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The technical product and end-use product, including formulants, were assessed against the contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern, Part 3 Contaminants of Health or Environmental Concern.* The PMRA has reached the following conclusions:

- Technical grade Mono- and Di-Potassium Salts of Phosphorous Acid and the end-use product Confine are not persistent and are not expected to bioaccumulate in the environment.

- Mono- and di-potassium salts of phosphorous acid does not meet the Track1 criteria and will not form any transformation products which meet the Track 1 criteria. Mono- and di-potassium salts of phosphorous acid is a naturally occurring substance and is not expected to be persistent or bioaccumulative in the environment.

- Technical grade Mono- and Di-Potassium Salts of phosphorous acid and the end-use product Confine are not persistent and are not expected to bioaccumulate in the environment and does not form any transformation products that meet the Track 1 criteria.

- There are no Track 1 formulants in the technical product or end-use product.

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

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, formulants and contaminants in the technical and end-use products are assessed against the formulants and contaminants identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*. This list of formulants and contaminants of health and environmental concern are identified using existing policies and regulations including: the federal Toxic Substances Management Policy; the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol); and the PMRA Formulants Policy as described in the PMRA Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document*. The *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* is maintained and used as described in the PMRA Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

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

- Part 1: Formulants of Health or Environmental Concern;
- Part 2: Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions; and
- Part 3: Contaminants of Health or Environmental Concern.

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

Technical grade Mono- and Di-Potassium Salts of Phosphorous Acid and the end-use product Confine are not persistent and are not expected to bioaccumulate in the environment. The end-use product Confine does not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

7.0 Summary

7.1 Human Health and Safety

The available information for mono- and di-potassium salts of phosphorous acid is adequate to qualitatively identify the toxicological hazards that may result from human exposure to mono- and di-potassium salts of phosphorous acid. Submitted information suggests that mono- and di-potassium salts of phosphorous acid is of low acute toxicity irrespective of the route of exposure and only minimally irritating to the eyes.

Occupational exposure is expected to be minimal resulting from the use pattern, method of application, and the application rate. Moreover, the precautionary statements on the product labels are sufficient to minimize any risk due to exposure of workers and bystanders.

Exposure to mono- and di-potassium salts of phosphorous acid from the diet or drinking water is not expected to be of concern.

7.2 Environmental Risk

Because mono- and di-potassium salts of phosphorous acid and the end-use product Confine fungicide are used post-harvest indoors, the risk to non-target organisms is considered to be negligible when used according to the label.

7.3 Value

Evidence from five trials on post-harvest treatment of potatoes was provided to support the claims. The results show that one application of Confine at the registered rate suppressed late blight and pink rot in stored potatoes.

Metalaxyl-M–sensitive or metalaxyl-M-resistant *P. erythroseptica* strains were controlled by phosphorous acid. Phosphorous acid did not affect tuber processing quality. The use of Confine fungicide resulted in darkening of lighter- skinned potatoes so the use has been limited to russet-coloured potatoes of potatoes intended for processing.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and in accordance with the Pest Control Products Regulations, has granted conditional registration for the sale and use of the technical grade active ingredient Mono- and Di-Potassium Salts of Phosphorous Acid and the end-use product Confine for suppression of late blight and pink rot on harvested potato tubers.

An evaluation of current scientific data from the applicant has resulted in the determination that, under the approved conditions of use, the end-use product has value and does not present an unacceptable risk to human health or the environment.

Although the risks and value have been determined to be acceptable when all risk reduction measures are followed, as a condition of these registrations, additional scientific information (listed below) is being requested from the registrant. For more details, refer to the Section 12 Notice associated with these conditional registrations

Chemistry

- Storage stability data for the end-use product representing at least one year of storage at ambient conditions
- Corrosion data for the end-use product representing at least one year of storage at ambient conditions

Value

- Additional trials are required to demonstrate that Confine fungicide will suppress late blight and pink rot of stored potatoes for up to 8 months.

NOTE: The PMRA will publish a Consultation Document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

List of Abbreviations

µg	micrograms
ADI	acceptable daily intake
ARfD	acute reference dose
BAF	bioaccumulation factor
BCF	bioconcentration factor
bw	body weight
CAS	chemical abstracts service
g	gram
hr	hour(s)
GRAS	Generally Regarded As Safe
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
mg	milligram
mL	millilitre
MAS	maximum average score
MIS	maximum irritation score
MOE	margin of exposure
nm	nanometre(s)
NOAEL	no observed adverse effect level
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
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 Di-Potassium Salts of Phosphorous Acid and Its Associated End-use Product (Confine)

STUDY	SPECIES, STRAIN AND DOSES	NOAEL & LOAEL mg/kg bw/day	TARGET ORGAN, SIGNIFICANT EFFECTS, COMMENTS
ACUTE STUDIES - TECHNICAL			
Oral	Sprague-Dawley rat (5/sex) Dose: 2000 mg/kg bw (limit test)	LD_{50} > 2000 mg/kg bw	No treatment related effects were observed. Potassium phosphite solution (42 %) was used.
Dermal	New Zealand white rabbits (5/sex) Dose: 5050 mg/kg bw (limit test)	LD_{50} > 5050 mg/kg bw	Transient erythema was observed. Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.
Inhalation	Sprague-Dawley albino rats (5/sex) Nominal conc: 5.61 mg/L Analytical conc: 2.02 mg/L	LC_{50} > 2.02 mg/L	No treatment related effects were observed. Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.
Skin Irritation	New Zealand white rabbits (2♂ & 1♀) Dose: 0.5 mL of test material	MAS (24, 48, & 72 hrs) of 0.0/8.0 Non-irritating	No treatment related effects were observed. Potassium phosphite solution (42 %) was used.
Eye Irritation	New Zealand white rabbits (1♂ & 2♀) Dose: 0.1 mL of test material	MIS (1 hr) of 5.33/110 MAS (24, 48, & 72 hrs) of 0.0/110 Minimally irritating	Minimum conjunctivae in 2/3 animals at 1 hr post-instillation. Resolved by 24 hrs post-instillation. Potassium phosphite solution (42 %) was used.
Skin Sensitization (Buehler Test Method)	Hartley-Albino guinea pigs (15/sex) Dose: 5/sex untreated control group & 10/sex treated with 0.4 mL (induction and challenge) of undiluted test material	Not a dermal sensitizer	No treatment related effects were observed. Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.
ACUTE STUDIES - FORMULATION *[Confine]*			
Oral	Sprague-Dawley rat (5/sex) Dose: 2000 mg/kg bw (limit test)	LD_{50} > 2000 mg/kg bw	No treatment related effects were observed. Potassium phosphite solution (42 %) was used.

STUDY	SPECIES, STRAIN AND DOSES	NOAEL & LOAEL mg/kg bw/day	TARGET ORGAN, SIGNIFICANT EFFECTS, COMMENTS
Dermal	New Zealand white rabbits (5/sex) Dose: 5050 mg/kg bw (limit test)	LD_{50} > 5050 mg/kg bw	Transient erythema was observed. Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.
Inhalation	Sprague-Dawley albino rats (5/sex) Nominal conc: 5.61 mg/L Analytical conc: 2.02 mg/L	LC_{50} > 2.02 mg/L	No treatment related effects were observed. Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.
Skin Irritation	New Zealand white rabbits (2♂ & 1♀) Dose: 0.5 mL of test material	MAS (24, 48, & 72 hrs) of 0.0/8.0 Non-irritating	No treatment related effects were observed. Potassium phosphite solution (42 %) was used.
Eye Irritation	New Zealand white rabbits (1♂ & 2♀) Dose: 0.1 mL of test material	MIS (1 hr) of 5.33/110 MAS (24, 48, & 72 hrs) of 0.0/110 Minimally irritating	Minimum conjunctivae in 2/3 animals at 1 hr post-instillation. Resolved by 24 hrs post-instillation. Potassium phosphite solution (42 %) was used.
Skin Sensitization (Buehler Test Method)	Hartley-Albino guinea pigs (15/sex) Dose: 5/sex untreated control group & 10/sex treated with 0.4 mL (induction and challenge) of undiluted test material	Not a dermal sensitizer	No treatment related effects were observed. Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.
SHORT-TERM TOXICITY			
90-day dietary	Sufficient information was available, as well as a history of safe use, to suggest that treatment-related effects would not be anticipated.		
REPRODUCTION AND DEVELOPMENTAL TOXICITY			
Developmental toxicity	Sufficient information was available, as well as a history of safe use, to suggest that treatment-related effects would not be anticipated.		
GENOTOXICITY			
STUDY	**SPECIES and STRAIN or CELL TYPE AND CONCENTRATIONS or DOSES**		**RESULTS**
Gene mutations in bacteria	*Salmonella typhimurium* strains TA 97, TA 98, TA 100, TA 1535 and TA 1537; *E. Coli* WP2uvrA 313−5000 μg/plate; with and without S9 activation		Negative Agri-Fos 400, which was tested, and is equivalent to Confine, contains 45.5 % mono- and di-potassium salt of phosphorous acid.

STUDY	SPECIES, STRAIN AND DOSES	NOAEL & LOAEL mg/kg bw/day	TARGET ORGAN, SIGNIFICANT EFFECTS, COMMENTS
Gene mutations in mammalian cells *in vitro*	Sufficient information was available, as well as a history of safe use, to suggest that treatment related effects would not be anticipated.		
Compound-Induced Mortality: None.			
Recommended ARfD: Due to the low toxicity and history of safe use, an ARfD was not determined.			
Recommended ADI: Due to the low toxicity and history of safe use, an ARfD was not determined. **MOE for other critical endpoint(s):** Due to the low toxicity and history of safe use, an MOE was not determined.			

Table 2 Use (label) Claims Proposed by Registrant and Whether Acceptable or Unsupported

Crop	Disease Rates, Use Pattern	Accepted VSAD Claims
Potatoes (in storage; russet-skinned and potatoes for processing only)	Pests: Pink rot (*P. erythroseptica*); late blight (*P. infestans*) Rate: 1:4.3 dilution; apply 2 L of the mixture to 1000 kg of harvested potatoes Method of application: spray Application timing: post-harvest No. of applications: 1 (per season)	The claim for suppression of pink rot and late blight of storage potatoes is conditionally supported based on trial results up to 77 days in storage. Additional data are required that demonstrate sustained disease control for up to 8 months.

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