PRVD2008-04

Proposed Re-evaluation Decision

2-Phenylphenol and Salts

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Overview

What is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobials 2-phenylphenol and its two sodium salts (sodium-o-phenylphenate and tetrahydrate), Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing 2-phenylphenol and salts for sale and use in Canada.

An evaluation of available scientific information found that all products containing 2-phenylphenol and salts do not present unacceptable risks to human health or to the environment when used according to label directions. As a condition of the continued registration of 2-phenylphenol and salts, new risk-reduction measures must be included on the labels of all products.

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment.

This proposal affects all end-use products containing 2-phenylphenol and salts registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for 2-phenylphenol and salts, and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides the detailed technical information on the assessment of 2-phenylphenol and salts.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

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

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

Health Canada's Pest Management Regulatory Agency (PMRA) is re-evaluating active ingredients and their uses to determine their continuing acceptability in relation to human health, the environment and value. 2-Phenylphenol is one of the active ingredients to be re-evaluated during the current re-evaluation cycle. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

2-Phenylphenol and salts have been re-evaluated under Re-evaluation Program 1, which relies as much as possible on foreign reviews, typically, United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, there must be a suitable foreign review that meets the following conditions:

- It covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions.
- It addresses the active ingredient and the main formulation types registered in Canada.
- It is relevant to registered Canadian uses.

Based on the outcome of foreign reviews, the PMRA is proposing, under Program 1, a regulatory decision and will require appropriate risk-reduction measures for Canadian uses of an active ingredient. In this proposed decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy (TSMP)). A review of the chemistry of Canadian products is also conducted.

The USEPA conducted a re-evaluation of 2-phenylphenol and salts, and conclusions of this re-evaluation are published in a 2006 RED. On the basis of health and environmental risk assessments, the USEPA concluded that 2-phenylphenol and salts were eligible for reregistration with implementation of risk-reduction measures. Based on the comparison of American and Canadian use patterns, the USEPA assessments described in this RED document were considered to be an adequate basis for the proposed Canadian re-evaluation decision.

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

What are 2-Phenylphenol and Salts?

2-Phenylphenol and its two sodium salts, sodium-o-phenylphenate and tetrahydrate, are antimicrobials that control microorganisms, including fungi, bacteria, mould and yeast. They are material preservative agents and are also used in the post-harvest treatment of fruits and vegetables. In Canada, 2-phenylphenol and salts (classified as use-site categories 12 and 18) are applied by dipping, fogging, flooding or spraying for post-harvest treatment of fruits and vegetables; painted on by brush, roller or airless sprayer; or added (open pour) as a material preservative (the products are used in items such as ceramic glazes, felt gaskets, paper dyes, laundry starch, concrete additives,

adhesives, paints, leather, textiles, metalworking fluids, fire extinguisher solutions, floor wax emulsions, chemical toilets, construction materials and polyvinyl alcohol).

All current uses are being supported by the registrants, except for the manufacturing use as a disinfectant (PCP #24934) and the post-harvest application on certain fruits and vegetables (i.e. apples, cantaloupes, cherries, peaches, plums, carrots, cucumbers, peppers and tomatoes). Only use on pears will remain on Canadian label and is included in this assessment.

Health Considerations

Can Approved Uses of 2-Phenylphenol and Salts Affect Human Health?

Additional risk-reduction measures are required on 2-phenylphenol and salts labels. 2-Phenylphenol and salts are unlikely to affect your health when used according to the revised label directions.

Exposure to 2-phenylphenol and salts may occur through consumption of food and water, working as a mixer/loader/applicator, or by entering treated sites. When assessing health risks, two key factors are considered: the levels at which no health effects occur, and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that 2-phenylphenol and salts were unlikely to affect human health, provided that risk-reduction measures were implemented. These conclusions were considered applicable to the Canadian situation, and equivalent risk-reduction measures are required.

Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

2-Phenylphenol and salts are currently registered in Canada for use on pears, apples, cantaloupes, cherries, peaches, plums, carrots, cucumbers, peppers, sweet potatoes and tomatoes. 2-phenylphenol and salts may be used on other crops in other countries that are imported into Canada. The Canadian MRLs established for 2-phenylphenol and salts are 10 ppm for citrus and 25 ppm for pears.

Environmental Considerations

What Happens When 2-Phenylphenol and Salts are Introduced Into the Environment?

Additional risk-reduction measures are required on the labels of products containing 2-phenylphenol and salts. 2-Phenylphenol and salts are unlikely to affect non-target organisms when used according to revised label directions.

The USEPA did not conduct a quantitative risk assessment. In toxicity studies, 2-phenylphenol and salts demonstrated low toxicity to birds, and moderate toxicity to mammals, freshwater fish, freshwater invertebrates, and algae. Based on environmental fate of 2-phenylphenol and salts, the USEPA believes that environmental exposure from use of 2-phenylphenol and salts is likely to be low. No data were required for an environmental quantitative assessment.

The USEPA concluded that the reregistration of 2-phenylphenol and salts was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions were considered to be applicable to the Canadian situation, and equivalent risk-reduction measures are required.

Measures to Minimize Risk

Registered pesticide product labels contain specific directions for use, which include risk-reduction measures to protect human and environmental health. These directions are required by law to be followed. As a result of the re-evaluation of 2-phenylphenol and salts, further risk-reduction measures are proposed in addition to those already identified on existing labels for products containing 2-phenylphenol and salts. These additional measures are designed to further protect human health and the environment and are summarized as follows:

Human Health

- to protect mixer/loader/applicators: additional protective equipment
- to protect consumers from postapplication exposure to textiles: additional advisory label statement

Environment

- to reduce potential surface water contamination: additional advisory label statement

Next Steps

Before making a final re-evaluation decision on 2-phenylphenol and salts, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document which will include the decision, the reasons for it, a summary of comments received on the proposed decision, and the PMRA's response to these comments.

[2] "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*

Science Evaluation

1.0 Introduction

2-phenylphenol and its salts, sodium-o-phenylphenate and tetrahydrate, are antimicrobials that control microorganisms including fungi, bacteria, mould and yeast. They are material preservative agents and used as a post-harvest treatment of fruits and vegetables.

Following the re-evaluation announcement for 2-phenylphenol and salts, the registrants of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses currently registered in Canada, except for the post-harvest application on certain fruits and vegetables: apples, cantaloupes, cherries, peaches, plums, carrots, cucumbers, peppers, sweet potatoes and tomatoes. Post-harvest application of pears is supported.

The PMRA used recent assessments of 2-phenylphenol and salts from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for 2-phenylphenol and salts, dated 2006, can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Active substance: Orthophenylphenol

Function: Fungicide

Chemical names:

IUPAC: biphenyl-2-ol

CAS: [1,1'-biphenyl]-2-ol

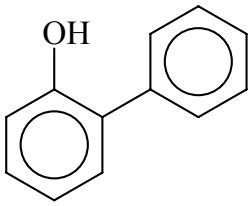
Chemical class: Phenol

CAS Number: 90-43-7

Molecular Formula: $C_{12}H_{10}O$

Molecular Weight: 170.2 amu

Structural Formula:



Based on the manufacturing process and the starting materials used, the product (PCP #22848) is not expected to contain impurities of human health or environmental concern as identified in Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy (TSMP) Track 1 substances as identified in Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, Appendix II.

2.2 Physiochemical Properties of Active Substance and Interpretation

Property	Result
Vapour pressure at 140°C	0.9 kPa
Henry's law constant 25°C	1.05×10^{-6} atm-m^3/mole
Ultraviolet (UV)/visible spectrum	not expected to absorb UV at $\lambda > 300$ nm
Solubility in water at 25°C	0.7 g/L
n-Octanol–water partition coefficient	log K_{ow} = 3.3
Dissociation constant at 25°C	pKa = 9.97

2.3 Comparison of Use Patterns in Canada and the United States

2-Phenylphenol and salts are material preservatives used to control microorganisms, including fungi, bacteria, mould and yeast. They are registered for use in Canada to control storage diseases of fruits and vegetables, and as a material preservative (the products are used in items such as ceramic glazes, felt gaskets, paper dyes, laundry starch, concrete additives, adhesives, paints, leather, textiles, metalworking fluids, fire extinguisher solutions, floor wax emulsions, chemical toilets, construction materials and polyvinyl alcohol). The percentage of 2-phenylphenol and salts in commercial products can range from 16.8% to 99.5%. The end-use products are formulated as solutions, particulate (flakes), dust or powders.

A comparison of U.S. and Canadian use patterns was conducted. The Canadian formulations, use sites, maximum application rates and application methods are encompassed by those of the U.S. Based on this comparison, it was concluded that the USEPA RED for 2-phenylphenol and salts is an adequate basis for the re-evaluation of Canadian uses of 2-phenylphenol and salts.

All current uses are being supported by the registrants, except for the manufacturing use as a disinfectant (PCP #24934) and the post-harvest application on certain fruits and vegetables (i.e. apples, cantaloupes, cherries, peaches, plums, carrots, cucumbers, peppers, sweet potatoes and tomatoes). Only use on pears will remain on the Canadian label and is included in this assessment. Appendix I lists all end-use products containing 2-phenylphenol and salts that are registered under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

The USEPA conducted a re-evaluation of 2-phenylphenol and salts and published their conclusions in a 2006 RED. In this document, it was concluded that the end-use products formulated with 2-phenylphenol and salts met the safety standard under the U.S. *Food Quality Protection Act* (FQPA) and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended labels of all end-use products containing 2-phenylphenol and salts.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to 2-phenylphenol and salts may occur through consumption of food and water, residential exposure, working as a mixer/loader/applicator or by entering treated sites. 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 (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but measures to mitigate (reduce) risk would be required. The toxicological endpoints selected by the USEPA for assessment of risk from occupational exposure are summarized in Appendix II, Table 1.

Workers can be exposed to 2-phenylphenol and salts through mixing, loading or applying the pesticide, and when re-entering a treated site to conduct activities.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

Thirty one dermal and inhalation exposure scenarios were identified by the USEPA. Among the scenarios assessed in the RED, the following six exposure scenarios were considered relevant to the Canadian situation:

1) Mixing/loading soluble concentrate (solid and liquid) using liquid open pour methods of adding preservative products to metalworking fluids, paint and textiles
2) Mixing/loading soluble concentrate (solid and liquid) using liquid pump methods of adding preservative products to metalworking fluids, paint, paper pulp and textiles
3) Handling solutions via mopping application
4) Handling paints via method of brush/roller and airless spraying applications
5) Mixing/loading liquid for automated post- harvest application on crops (citrus and pears)
6) Automated application process for crops (citrus and pears)

Handler exposure analyses were performed using the Pesticide Handlers Exposure Database (PHED), Version 1.1. The assessment was based on different application sites with the application rate ranging from 0.00012% a.i. (for application to outdoor hard surfaces) to 5.66% a.i. (for preservation of metalworking fluid). Based on a 21-day rat dermal toxicological study, a dermal no observed adverse effect level (NOAEL) of 100 mg/kg/day was used to assess short-term risk via the dermal route of exposure. No inhalation and intermediate-term dermal toxicological studies were available. Therefore, an oral NOAEL of 100 mg/kg/day based on developmental (gavage) toxicity studies in rat and rabbits was used to assess for short-term inhalation risk, and an oral NOAEL of 39 mg kg/day based on a combined oral toxicity/carcinogenicity study in rats was used to assess both intermediate-term dermal and inhalation risk. A human dermal absorption factor of 43% was used. Inhalation absorption was assumed to be equivalent to oral absorption. A margin of exposure of 100 was considered acceptable for short- and intermediate-term exposures. Other assumptions included a default average adult body weight of 70 kg, and a typical workday of 8 hours per day.

The USEPA reported acceptable short- and intermediate-term dermal and inhalation risks for workers wearing a long-sleeved shirt, long pants and chemical-resistant gloves for all of the above scenarios, with MOEs ranging from 140 to 120 000, except for the liquid open pour method and paint application via an airless sprayer. To mitigate the exposure risk, the USEPA required the following label statement: Workers must wear a long-sleeved shirt, long pants and chemical-resistant gloves when handling.

For the scenario of the liquid open pour method (adding preservative product to textiles), the short-term dermal MOE was 90 (target MOE = 100) and intermediate-term dermal MOE was 78 (with baseline personal protective equipment (PPE) and chemical-resistant gloves). However, the USEPA determined that these values were based on conservative estimates and the daily dosages calculated were most likely overestimated. The USEPA concluded that, if scenarios or specific values were available, then the MOEs would be expected to be greater than 100 and were not of concern. Therefore, no further mitigation was required for this scenario.

For the scenario of workers applying 2-phenylphenol-containing paints through the use of an airless sprayer, the risk was of concern for short-term inhalation exposure with an MOE of 43. The short-term dermal MOE of 180 was acceptable when workers wore gloves. The intermediate-term exposure was not assessed by the USEPA because it was assumed that 2-phenylphenol and salts treated paint was not used on a continuous basis by professional painters. To mitigate the short-term inhalation exposure risk, the USEPA determined that for products containing 2-phenylphenol and salts and used as a paint preservative (with an airless sprayer) the maximum application rate of 2-phenylphenol and salts must be less than 0.33% a.i. to address risks for workers applying paint. This will result in MOEs that are above the target of 100. The Canadian maximum application rate for painting is 0.386% a.i. Therefore, no further mitigation is required for this use in Canada.

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of products containing 2-phenylphenol and salts. Conclusions derived from the RED are considered applicable to the Canadian situation. The current Canadian labels read as follows:

- **PCP #27633**
  Wear coveralls over long sleeved shirt and long pants, chemical resistant gloves, socks and chemical resistant footwear during mixing, loading, application, clean-up and repair, and wear goggles or face shield, during mixing or loading.

- **PCP #27893 and PCP #27862**
  Wear goggles or face shield when handling, wear protective clothing and rubber gloves.

- **PCP #24943**
  Wear a respirator, goggles or face shield and gloves when handling product.

In addition to the PPE already on the labels, the PMRA requires the following:

- Wear a long-sleeved shirt, long pants and chemical-resistant gloves when handling product.

Proposed label amendments are listed in Appendix III.

3.1.1.2 Postapplication Exposure and Risk

The postapplication occupational risk assessment considered exposures to workers entering treated sites. Based on the use pattern of 2-phenylphenol and salts, workers could be exposed to residues after the product is applied. Four scenarios were identified. Among the scenarios assessed in the RED, the following two scenarios were considered relevant to the Canadian situation:

1) Handling treated metalworking fluid by machinist

The dermal exposure assessment was based on the two-hand immersion model from ChemSTEER using the typical application rate of 1.5% a.i. A surface area of both hands of 840 cm^2, an adult body weight of 70 kg, a default dermal absorption rate of 43% and one exposure event per day were assumed. The assessment was based on a short-term NOAEL of 100 mg/kg/day, and intermediate- and long-term NOAEL of 39 mg/kg/day for dermal exposure. The dermal MOE was 290 for intermediate- and long-term exposure, and the short-term dermal MOE was 54, which was below the target MOE of 100 and of concern. To mitigate the occupational postapplication (short-term dermal) exposure risk, the USEPA determined that all products used as a metalworking fluid must not exceed a maximum application rate of 0.6% a.i. This will result in MOEs that are above the target of 100. The maximum application rate currently used in Canada for metalworking fluid is 0.622% a.i. Therefore, no additional mitigation measures are required.

The inhalation exposure assessment was based on a screening-level inhalation exposure estimate using the OSHA PEL for oil mist. The high-end oil mist concentration was based on 5 mg/m^3, the inhalation rate for a machinist was assumed to be 1.25 m^3/hr, and a worker was assumed to be exposed to the metalworking fluid 8 hours a day, for 5 days a week. The assessment was based on a short-term NOAEL of 100 mg/kg/day, and an intermediate- and long-term NOAEL of 39 mg/kg/day for inhalation exposure. The MOE was 9300 for short-term inhalation exposure 3600 for intermediate- and long-term exposure, which were not of concern.

2) Post-harvest application on pears and citrus:

Workers performing sorting and packing activities with pears and citrus fruits are potentially exposed to 2-phenylphenol and salts following application. Potential dermal and inhalation exposures also exist for storage room re-entry workers following thermo-fogging applications, post-treatment residue sampling and the transporting of treated pears from storage to places where they are processed and distributed. An application rate of 2% was used for the risk assessment. The short- and intermediate-term mean dermal and inhalation MOEs for both sorting and packing were found to be acceptable (MOEs ranging from 120 to 7300 for pears and 770 to 11 000 for citrus).

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of 2-phenylphenol and salts, and conclusions derived from the RED are considered applicable to the Canadian situation. No further mitigation measures are required.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach as explained for occupational exposure and risk assessment in Section 3.1.1. The toxicological endpoint selected by the USEPA for assessment of risk from residential exposure is summarized in Appendix II, Table 1.

Homeowners can be exposed to 2-phenylphenol and salts through mixing, loading and applying the pesticide, and when re-entering a treated site. Toddlers can be exposed via "hand-to-mouth" and "object-to-mouth" activities and through incidental ingestion of the product.

In the U.S., four residential application scenarios were identified. Among the scenarios assessed in the RED, the following three scenarios were considered relevant to the Canadian situation:

- Application to indoor hard surfaces via mopping
- Painting via brush or roller application
- Painting via airless sprayer application

The assessment was based on the Pesticide Handler Exposure Database (PHED), using the rate of 0.56% a.i. for painting with a brush or roller and airless sprayer applications. Residential handler short-term dermal MOEs (ranging from 110 to 780) and inhalation MOEs (ranging from 10 000 to 220 000) were found to be acceptable for all scenarios assessed. The USEPA also conducted an assessment of the vapour portion of the inhalation exposure of residential painters. The Wall Paint Exposure Model (WPEM), Version 3.2 was used to estimate air concentrations resulting from the use of paint preserved with 2-phenylphenol. WPEM was developed to allow the USEPA to estimate potential air concentrations and consumer/worker exposures to chemicals emitted from wall paint which is applied using a roller or a brush. Results of the WPEM model calculated a short-term vapour inhalation MOE of 1500, which does not present a concern for residential painters.

Among the residential postapplication scenarios assessed in the RED, the following exposure scenarios were considered relevant to the Canadian use pattern:

- children contacting treated hard surface/floors;
- infants mouthing treated textiles;
- exposure for adults and children in areas painted with preserved paint;
- wearing treated clothing.

The scenarios were assessed as follows:

- For the scenario of children contacting treated hard surface/floors, dermal exposures and MOEs were calculated for children contacting treated hard surface floors in residential homes (short-term) and in commercial daycare centres (intermediate-term). Toddlers (3 years old) were used to represent the 1-to-6-year-old age group and were assumed to weigh 15 kg. The application rates used in the scenarios were 0.00006 g a.i./cm² (0.000126 lb a.i./ft²) and 0.000009 g a.i./cm² (0.0000183 lb a.i./ft²) for the short and intermediate terms, respectively.

- For the scenario of an infant mouthing treated textiles, the same assumptions were used as above. Oral exposure was calculated for children in residential settings (short-term) and in commercial daycare centres (intermediate-term). The application rate was 0.249% a.i.

- In the scenario of exposure to adults and children in areas painted with preserved paint, WPEM default scenarios were used to determine exposure to adults and children. An exposure duration of 24 hrs/day and inhalation rates of 0.5 m³/hr and 0.4 m³/hr for the adult and child were assumed. The adult and child were assumed to be in a non-painted part of the house while a bedroom was being painted by a professional painter.

- The scenario of children and adults wearing treated clothing was based on clothing treated with a trigger-pump spray (i.e. homeowner use), which was identified as a worst case scenario. It was assumed that wearing treated clothing would be for short-term exposure (16 hours/day). Calculations were based on both a 100% and 5% transfer factor and a guarantee of 0.249% a.i. The USEPA calculated a concentration on clothing of 0.493 mg a.i./cm² based on surrogate data, using absorbent material with a product absorption rate of 198 mg/cm². For the scenario of exposure for adults and children in areas painted with preserved paint, WPEM default scenarios were used to determine exposure. An exposure duration of 24 hrs/day and inhalation rates of 0.5 m³/hr and 0.4 m³/hr for adult and child, respectively, were assumed. The adult and child were assumed to be in a non-painted part of the house while a bedroom was being painted by a professional painter.

Residential postapplication dermal and inhalation MOEs (ranging from 120 to 6900) were found to be acceptable for all scenarios assessed, except for children and adults wearing treated clothing (MOE < 1 for children and MOE = 1 for adults based on a 100% transfer factor, and MOE = 16 for children and MOE = 25 for adults based on a transfer factor of 5%). The USEPA determined that adding clear instructions for washing and rinsing textile items would result in adequate removal of residues from the treated items and address concerns regarding this scenario. As a result, to mitigate the risk of dermal exposure to treated clothing, the USEPA required that for both factory textile use and ready-to-use, trigger-pump spray (homeowner) on textiles, all labels for laundered textile use must have directions indicating that the items must be treated prior to washing and rinsing.

The RED adequately addressed potential exposure scenarios associated with the Canadian residential uses of 2-phenylphenol and salts (i.e. use in paints, textiles, cleaning solutions), and thus conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires a mitigation measure (for the product with textile use) to protect consumers from postapplication exposure to textiles as follows:

- All textiles must be washed before manufacturing clothing.

Proposed label amendments are listed in Appendix III.

3.1.2.2 Exposure from Food and Drinking Water

No acute endpoints of concern were identified by the USEPA, and 2-phenylphenol and salts were classified as "not likely to be carcinogenic to humans". On this basis, no acute or cancer risk assessments were conducted.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it was expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix II, Table 1).

Exposure from drinking water was not assessed by the USEPA. Based on the use pattern on 2-phenylphenol and salts and their tendency to degrade rapidly in the environment, the USEPA believed that 2-phenylphenol and salts were not likely to be present in drinking water sources at a substantial concentration. Therefore, risks from the drinking water were not of concern, and a quantitative drinking water assessment was not required by the USEPA.

An unrefined Tier I chronic dietary risk assessment due to food was conducted by the USEPA using the Dietary Exposure Evaluation Model (DEEM-FCID™), Version 2.03, as well as Lifeline Model, Version 3.0, which uses food consumption data from the U.S. Department of Agriculture's Continuing Survey of Food Intake by Individuals (CSFII) from 1994 to 1996 and 1998. The chronic reference dose was 0.39 mg/kg/day based on a combined oral toxicity/carcinogenicity study in rats (NOAEL = 39 mg/kg/day) and a FQPA safety factor of 1×. It was assumed that 100% of each commodity was treated and that all residues were at tolerance levels. The result from exposure to food alone was estimated below the level of concern (4.4% of cPAD, <100%) for the general U.S. population and all other population subgroups (the most highly exposed being children 1 to 2 years old with 15.8% of the cPAD). No mitigation with respect to dietary risk was required.

The registered use in Canada (on pears) was included in the USEPA risk assessment, and Canadian maximum application rates are encompassed by those of the United States. Therefore, the USEPA assessment is applicable to the Canadian situation.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to 2-phenylphenol and salts (i.e. from food, water and residential exposures). Potential exposures from food and residential scenarios were considered and aggregated for 2-phenylphenol and its salts.

The USEPA concluded that the aggregate dietary risk (food only), and the residential handler dermal and inhalation risks did not exceed the level of concern. Therefore, no risk mitigation measures were required to address these exposure scenarios.

However, risks of concern were identified for the postapplication exposure scenario of child and adult dermal exposure to treated clothing. To mitigate the exposure, a label amendment is proposed and is listed in Appendix III.

The Canadian potential aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of 2-phenylphenol and salts in Canada.

3.1.3 Cumulative Effects

The USEPA has not determined whether 2-phenylphenol and salts have a common mechanism of toxicity with other substances or whether they share a toxic metabolite produced by other substances. Therefore, it was assumed that 2-phenylphenol and salts do not share a common mechanism of toxicity with other substances and a cumulative risk assessment was not required. The USEPA assessment is applicable for the Canadian situation.

3.2 Environment

3.2.1 Environmental Risk Assessment

2-Phenylphenol was stable to hydrolysis at pHs of 5, 7 and 9. It was reported that the UV absorption spectrum was less than 290 nm, which indicates a limited potential for phototransformation. However, 2-phenylphenol in a neutral aqueous medium was found to be photolytically unstable as it degraded completely in 14 days when exposed to sunlight. When exposed to UV light (235.7 nm), it degraded into phenyl benzoquinone, phenylhydroquinone, and 2-hydroxy benzofuran. Its major transformation pathway was through biotransformation under aerobic and anaerobic conditions (the observed half-life varies from a few hours to three weeks).

2-Phenylphenol and its salts were immobile in soils with a high K_{oc} value of 10 000, and were not likely to leach to groundwater or contaminate surface water through runoff.

The estimated log K_{ow} of 2-phenylphenol was 3.3, which indicates a potential to bioaccumulate in aquatic organisms.

From toxicity studies, 2-phenylphenol and salts demonstrated low toxicity to birds, and moderate toxicity to mammals, freshwater fish, freshwater invertebrates, and algae.

The USEPA did not conduct a quantitative ecological risk assessment. Based on use patterns, the USEPA concluded that indoor uses of 2-phenylphenol and salts were not likely to result in unacceptable ecological risk to non-target organisms, as the environmental exposure from indoor uses of 2-phenylphenol and salts is likely to be low. No further data were required by the USEPA for the quantitative risk assessment. In order to reduce ecological exposure, the USEPA required the following:

- Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or other waters.
- Do not discharge effluent containing this product to sewer systems.

Conclusions derived from the USEPA RED are considered relevant to the Canadian situation. Based on the RED and in consideration of the Canadian use pattern, the PMRA requires the following label statement on all Canadian labels:

- DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could be harmful to the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal Toxic Substances Management Policy and the Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of 2-phenylphenol and the following conclusions were made:

- 2-Phenylphenol is not bioaccumulative; the *n*-octanol–water partition coefficient (log K_{ow}) is 3.3, which is below the TSMP Track 1 cut-off criterion ($\geq$5.0).
  2-phenylphenol was not found to be persistent; the half-life for aerobic soil ranges from a few hours to three weeks, which is below the TSMP Track 1 criterion of 180 days.
  2-phenylphenol does not meet all Track 1 criteria, and thus they are not a candidate for Track 1 classification.

- Based on a review of the available chemistry information (see Section 2.1), the technical product is not expected to contain impurities of toxicological concern as identified in Regulatory Directive DIR98-04 or TSMP Track 1 substances as identified in Regulatory Directive DIR99-03, Appendix II.

- No other impurities of toxicological concern as identified in Section 2.13.4 of Regulatory Directive DIR98-04 or TSMP Track1 substances as identified in Appendix II of Regulatory Directive DIR99-03 are expected to be present in the technical product of 2-phenylphenol.

4.0 OECD Status of 2-Phenylphenol and Salts

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 30 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies. They compare experiences, share information and analyses, seek answers to common problems, and work to co-ordinate domestic and international policies to allow for consistency in practices across nations.

Based on the current available information on the status of 2-phenylphenol and salts in other OECD member countries, 2-phenylphenol and salts have been prohibited in Sweden since 1991, because of carcinogenic effects in experimental animals and a risk of potential exposure during handling.[3]

2-Phenylphenol and salts are registered in Australia and are currently pending review in the European Union. As described earlier, the United States, also an OECD member, assessed the registration of all uses of 2-phenylphenol and salts in 2006 and concluded that using 2-phenylphenol and salts as pesticides does not result in unreasonable adverse effects to human health, provided the risk-reduction measures recommended in the RED document are implemented. 2-Phenylphenol and salts are classified as "not likely to be carcinogenic to humans" in the USEPA RED document. The Canadian re-evaluation of 2-phenylphenol and salts is largely based on the 2006 USEPA assessment. As described in Section 3.2.2 above, the PMRA has found the USEPA human health risk conclusions to be relevant to the uses of 2-phenylphenol and salts in Canada and requires measures to mitigate potential human health. Therefore, concerns identified in Sweden relating to human health effects of the active ingredient were taken into consideration in the re-evaluation of 2-phenylphenol and salts in Canada and have been addressed in the proposed Canadian re-evaluation decision.

[3] "Swedish Chemicals Agency's Regulations on Chemical Products and Biotechnical Organisms (KIFS 1998:8), Appendix 5.

5.0 Proposed Re-evaluation Decision

The PMRA has determined that 2-phenylphenol and salts are acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use products must be amended to include the label statement listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

The Canadian registrants of the TGAIs have indicated that use of 2-phenylphenol and salts on post-harvest treatment of apples, cantaloupes, cherries, peaches, plums, carrots, cucumbers, peppers, sweet potatoes and tomatoes will no longer be supported in Canada. This re-evaluation decision is proposed only for use in the post-harvest treatment of pears and as a material preservative.

6.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 613-736-3799 outside Canada (long distance charges apply); Fax: 613-736-3798;
E-mail: pmra_infoserv@hc-sc.gc.ca.

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

The USEPA RED document (2-phenylphenol and salts, EPA Case No. 2575) is available on the Office of Pesticide Programs website at www.epa.gov/pesticides/reregistration under Chemical Status.

List of Abbreviations

µg	microgram
a.i.	active ingredient
ADI	acceptable daily intake
aPAD	acute population adjusted dose
bw	body weight
CAS	Chemical Abstracts Service
cPAD	chronic population adjusted dose
CSFII	Continuing Survey of Food Intakes by Individuals
DEEM	Dietary Exposure Evaluation Model (a modelling program)
DWLOC	drinking water level of concern
EDWC	estimated drinking water concentration
EEC	estimated environmental concentration
FIRST	FQPA Index Reservoir Screening Tool (a modelling program)
FQPA	*Food Quality Protection Act*
g	gram
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{oc}	organic carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre
LC_{50}	median lethal concentration
LOC	level of concern
LOD	limit of detection
LOAEL	lowest observed adverse effect level
mg	milligram
ml	millilitre
MOE	margin of exposure
MRL	maximum residue limit
nm	nanometre
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
OECD	Organisation for Economic Co-operation and Development
pH	-log10 hydrogen ion concentration
PCP	Pest Control Product
PHED	Pesticide Handlers Exposure Database
pKa	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
RED	Re-registration Eligibility Decision
REI	restricted entry interval
RQ	risk quotient
SCI-GROW	Screening Concentration In Ground Water (a modelling program)
TGAI	technical grade active ingredient

TSMP	Toxic Substance Management Policy
U.S.	United States
USEPA	United States Environmental Protection Agency
UV	ultraviolet
WPEM	Wall Paint Exposure Model

Appendix I Registered Products Containing 2 -Phenylphenol and Salts as of October 2007

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
11980	Technical	Dow Chemical Canada Inc.	Dowicide* 1 Technical	Solution	99.5%
27893	Commercial	Dow Chemical Canada Inc.	Dowicide* 1 Antimicrobial	Dust or Powder	99.5%
22848	Technical	Lanxess Corporation	Preventol O Extra	Solution	99.9%
24934	Commercial	Lanxess Corporation	Preventol O Extra Preservative	Particulate	99.5%
27633	Commercial	Lanxess Corporation	Preventol On Extra Preservative Solution	Solution	16.8% Present as Sodium-2-phenylphenol
11991	Technical	Dow Chemical Canada Inc.	Dowicide A Technical	Dust or Powder	71.7% Present as Tetrahydrate
27862	Commercial	Dow Chemical Canada Inc.	Dowicide A Antimicrobial	Dust or Powder	71.7% Present as Tetrahydrate
24697	Manufacturing Concentrate	Lanxess Corporation	Preventol ON Extra Antimicrobial Flake	Solution	63.3%

Appendix II Toxicological Endpoints for 2-Phenylphenol Health Risk Assessments

Table 1 Toxicological Endpoints Selected by the USEPA for 2-Phenylphenol Health Risk Assessments

Exposure Scenario	Dose (mg/kg bw/day)	Study	UF/SF or MOE[a]
Incidental Oral Short-Term (1–30 days)	**NOAEL** (maternal) = 100 mg/kg/day	Developmental (gavage) toxicity studies in rats and rabbits	100
Incidental Oral Intermediate-Term (1–2 months)	**NOAEL =** 39 mg/kg/day	Combined oral toxicity/carcinogenicity study in rats	100
Dermal Short-Term (1–30 days) (residential and occupational)	**NOAEL (**dermal) = 100 mg/kg/day (200 µg/cm^2)	21-day dermal toxicity study in rats	100
Dermal Intermediate- and Long-Term (1–6 months and > 6 months) (residential and occupational)	**NOAEL** = 39 mg/kg/day	Combined oral toxicity/carcinogenicity study in rats	100
Inhalation Short-Term (1–30 days) (residential and occupational)	**NOAEL (maternal)** = 100 mg/kg/day	Developmental (gavage) toxicity studies in rats and rabbits	100
Inhalation Intermediate- and Long-Term (1–6 months and > 6 months) (residential and occupational)	**NOAEL** = 39 mg/kg/day	Combined oral toxicity/carcinogenicity study in rats	100
Cancer (oral, dermal, inhalation)	Classification: Orthophenylphenol is classified as "Not likely to be carcinogenic below a specific dose range," without quantification of risk.		

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

Appendix III Label Amendments for Products Containing 2-phenylphenol and Salts

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

I) The following statement must be included in a section entitled **PRECAUTIONS,** in addition to the PPE currently listed in each label.

- Wear a long-sleeved shirt, long pants and chemical-resistant gloves when handling product.

II) For the label with textile use (PCP #27862), the following statement must be included in a section entitled **DIRECTIONS FOR USE**.

- All preserved textiles must be washed before manufacturing clothing.

III) The following statement must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

DO NOT discharge effluent containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans or other waters.

IV) Delete the following uses from the labels:

- Post-harvest treatment on fruits including apples, cantaloupes, cherries, peaches, plums, carrots, cucumbers, peppers, sweet potatoes and tomatoes.

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.