Proposed Re-evaluation Decision PRVD2013-03

p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate

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Table of Contents

Overview 1
What Is the Proposed Re-evaluation Decision? 1
What Does Health Canada Consider When Making a Re-evaluation Decision? 1
What are p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate? 2
Health Considerations 2
Environmental Considerations 3
Measures to Minimize Risk 3
Next Steps 3
Science Evaluation 5
1.0 Introduction 5
2.0 The Technical Grade Active Ingredient and Its Properties 5
2.1 Identity of the Technical Grade Active Ingredients 5
2.2 Physical and Chemical Properties 6
2.3 Description of Registered p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Use 6
3.0 Human Health 7
3.1 Toxicology Profile of p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate 8
3.2 Occupational Exposure 9
3.2.1 Chemical Handler Exposure and Risk 9
3.2.2 Postapplication Exposure and Risk 10
3.3 Non-Occupational Exposure 11
3.3.1 Residential Exposure and Risk 11
3.3.2 Residue Limits in Food Commodities 11
3.3.3 Dietary Exposure and Risk 11
3.3.4 Aggregate Exposure and Risk 11
3.3.5 Cumulative Exposure and Risk 12
4.0 Environment 12
4.1 Environmental Fate 12
4.2 Environmental Exposure and Risk Assessment 12
5.0 Value 12
6.0 Pest Control Product Policy Considerations 13
6.1 Toxic Substances Management Policy Considerations 13
6.2. Contaminants and Formulants of Health or Environmental Concern 13
7.0 Incident Reports 14
8.0 Organisation for Economic Co-operation and Development Status 14
9.0 Proposed Re-evaluation Decision 15
10.0 Supporting Documentation 15

List of Abbreviations 17
Appendix I Registered p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Products as of 17 July 2013 19
Table 1 p-Chloro-m-cresolate Products 19
Table 2 Sodium p-Chloro-m-cresolate Products 19
Appendix II Toxicological Endpoint for p-Chloro-m-cresol Human Health Risk 21
Appendix III Label Amendments for Products Containing p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate 23
References 25

Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobial active ingredients 3-methyl-4-chlorophenol, hereafter referred to as p-chloro-m-cresol, and 4-chloro-3-methylphenol, hereafter referred to as sodium p-chloro-m-cresolate, 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 p-chloro-m-cresol and sodium p-chloro-m-cresolate for sale and use in Canada.

An evaluation of available scientific information found that products containing p-chloro-m-cresol and sodium p-chloro-m-cresolate do not present unacceptable risks to human health or the environment when used according to the revised label directions. As a condition of the continued registration of p-chloro-m-cresol and sodium p-chloro-m-cresolate uses, new risk-reduction measures are proposed to be included on the labels of all products.

This proposal affects all end-use products containing p-chloro-m-cresol and sodium p-chloro-m-cresolate 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 p-chloro-m-cresol and sodium p-chloro-m-cresolate 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 detailed technical information on the assessment of p-chloro-m-cresol and sodium p-chloro-m-cresolate.

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).

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

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, presents the details of the cyclical re-evaluation approach.

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

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

What are p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate?

p-Chloro-m-cresol and sodium p-chloro-m-cresolate are broad-spectrum antimicrobial active ingredients used as material preservatives in industrial settings. These active ingredients are used in the preservation of adhesives and glues; joint cements; polymer dispersions and emulsions; metalworking fluids (ready-to-use and concentrates); building materials; coating materials; textile, paper, photo, printing and oil industries; leather at all stages of production; and additional materials including polishing and wax materials, and cleaning solutions. The commercial end-use products containing p-chloro-m-cresol and sodium p-chloro-m-cresolate can be applied in industrial settings using open or closed system technology. There are other non-pesticidal uses for p-Chloro-m-cresol and sodium p-chloro-m-cresolate, however, this document pertains to the pesticide uses only.

Health Considerations

Can Approved Uses of p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Affect Human Health?

p-Chloro-m-cresol and sodium p-chloro-m-cresolate are unlikely to affect your health when used according to the revised label directions.

Potential exposure to p-chloro-m-cresol and sodium p-chloro-m-cresolate may occur when applying the product in industrial settings and/or when coming in contact with treated materials/products. In Canada, p-chloro-m-cresol and sodium p-chloro-m-cresolate are not registered for food use and they are not authorized for use in food contact materials. Based on the registered use pattern, exposure from drinking water is expected to be limited.

The PMRA considers two key factors when assessing health risks: 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 (for example, children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Risks for human health are not of concern under current conditions of use. However, based on severe eye and skin irritation properties of p-chloro-m-cresol additional personal protective equipment is proposed for workers during handling, clean up, and repair activities.

Environmental Considerations

What Happens When p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Are Introduced Into the Environment?

p-Chloro-m-cresol and sodium p-chloro-m-cresolate are unlikely to affect non-target organisms when used according to the revised label directions.

Based on the currently registered use pattern in Canada, the PMRA concluded that p-chloro-m-cresol and sodium p-chloro-m-cresolate are unlikely to cause harm to the environment. Standard environmental advisory label statements to minimize surface water contamination are proposed.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of p-chloro-m-cresol and sodium p-chloro-m-cresolate, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Additional personal protective equipment to protect workers in industrial settings

Environment

- Standard advisory label statements to minimize surface water contamination
- A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision.

Next Steps

Before making a final re-evaluation decision on p-chloro-m-cresol and sodium p-chloro-m-cresolate, 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] that 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

p-Chloro-m-cresol and sodium p-chloro-m-cresolate are broad-spectrum antimicrobial active ingredients used as material preservatives.

In Canada, these antimicrobial active ingredients were first registered in 1998 and, therefore, are subject to re-evaluation according to Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*.

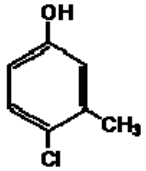
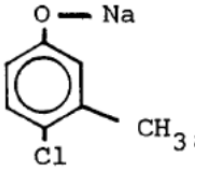
Following the re-evaluation announcement, the registrant of the technical grade active ingredients indicated their intention to support all currently registered uses of these active ingredients.

The proposed re-evaluation decision for p-chloro-m-cresol and sodium p-chloro-m-cresolate is based on the available assessments for these active ingredients conducted by the PMRA. In this proposed decision, the PMRA has taken into account the current policies including the federal Toxic Substances Management Policy.

2.0 The Technical Grade Active Ingredient and Its Properties

2.1 Identity of the Technical Grade Active Ingredients

			p-Chloro-m-cresol	Sodium p-Chloro-m-cresolate
Common name			parachlorocresol	4-chloro-3-methylphenol (sodium salt)
Function			Material Preservative	Hard-surface disinfectant and material preservative
Chemical Family			Chlorinated phenol	Chlorinated phenol
Chemical name	**1**	**International Union of Pure and Applied Chemistry (IUPAC)**	4-chloro-3-methylphenol	4-chloro-3-methylphenol (sodium salt)
	2	**Chemical Abstracts Service (CAS)**	4-chloro-3-methylphenol	Phenol, 4-chloro-3-methyl-, sodium salt (1:1)
CAS Registry Number			59-50-7	15733-22-9
Molecular Formula			C_7H_7ClO	C_7H_6ClNaO

	p-Chloro-m-cresol	Sodium p-Chloro-m-cresolate
Structural Formula		
Molecular Weight	142.58	164.6

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including Toxic Substances Management Policy Track 1 substances, are not expected to be present in the products.

2.2 Physical and Chemical Properties

Property	p-Chloro-m-cresol	Sodium p-Chloro-m-cresolate
Vapour pressure	8 Pa at 20°C	< 0.1 Pa at 100°C
Ultraviolet (UV) / visible spectrum	λ_{max} = ~ 220 nm λ = ~ 270 nm	λ_{max} = ~ 230 nm λ = ~ 280 nm
Solubility in water	4 g/L at 20°C	580 g/L
n-Octanol/water partition coefficient	Not on file	A low value for the octanol / water partition coefficient is expected since it is an ionic salt.
Dissociation constant	9.4	9.4

2.3 Description of Registered p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Use

Products containing p-chloro-m-cresol and sodium p-chloro-m-cresolate currently registered under the *Pest Control Products Act* are listed in Appendix I. All current uses are being supported by the registrant and, therefore, were considered in the re-evaluation of these active ingredients.

p-Chloro-m-cresol and sodium p-chloro-m-cresolate are used in the preservation of adhesives and glues; joint cements; polymer dispersions and emulsions; metalworking fluids (ready-to-use and concentrates); building materials; coating materials; textile, paper, photo, printing and oil industries; leather at all stages of production; and additional materials including polishing and wax materials, and cleaning solutions. The only difference between these active ingredients is due to their solubility, the phenol form (p-chloro-m-cresol) is oil soluble, while the phenate form (sodium p-chloro-m-cresolate) is water-soluble. Both can be applied at the registered concentration range using open or closed system technology. The current Canadian use patterns for p-chloro-m-cresol and sodium p-chloro-m-cresolate are summarized in Table 1 below.

Table 1 Summary of p-Chloro-m-cresol and Sodium p-Chloro-cresolate Use Patterns

	p-Chloro-m-cresol	Sodium p-Chloro-m-cresolate
Use Site Category	USC #18: Material: Material Preservative	
Formulation	Pellet (99.8%)	Flakes (99.4%) Solution (40%)*
Maximum Application Rate		
Adhesives and glues	1.00%	1.00%
Joint cements	0.20%	0.20%
Polymer dispersions and emulsions	0.20%	0.20%
Leather industry	0.40%	0.40%
Metalworking fluids		
• concentrates	3.00%	3.00%
• ready-to-use	0.20%	0.20%
Printing industry	0.30%	0.35%
Building materials (for example, concrete additives)	0.40%	0.40%
Coating materials (for example, paints)	0.40%	0.56%
Paper industry (for example, starch and pigment slurries)	0.30%	0.30%
Textiles industry (for example, spinning preparations)	2.00%	2.00%
Photo industry	0.20%	0.20%
Oil industry (for example, drilling muds)	2.00%	2.00%
Polishing and wax materials	0.40%	0.40%
Protein solutions	0.30%	0.42%
Cleaning solutions, detergents	0.20%	0.20%
Ceramic glazes	0.20%	0.25%
Fire extinguishing materials	0.30%	0.30%
Application methods	Open pour or closed system technology	

* Calculated as p-chloro-m-cresol

3.0 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which 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 p-chloro-m-cresol and sodium p-chloro-m-cresolate may occur while applying the pesticide in industrial settings and/or through contact with products/materials treated with these active ingredients. When assessing health risks, the PMRA considers two key factors: 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 (for example, children and nursing mothers).

3.1 Toxicology Profile of p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate

The toxicology databases for p-chloro-m-cresol and sodium p-chloro-m-cresolate were bridged based on the fact that in neutral conditions sodium p-chloro-m-cresolate converts completely to the phenolic form (p-chloro-m-cresol), and any potential systemic toxicity would be a result of exposure to the phenolic form, independent of the form administered in the toxicology studies.

The review of the p-chloro-m-cresol database conducted at the time of the initial registration revealed a low order of acute oral toxicity in rats and, of acute dermal toxicity in both rats and rabbits. A waiver for acute inhalation toxicity was supported based on particle size (flakes) of p-chloro-m-cresol. The active ingredient was found to be a severe irritant to rabbit eyes and skin (with corneal- and skin-corroding properties), and was considered to be a potential sensitizer in guinea pigs. The required hazard warning statements are included on the current end-use product labels.

No target organs were identified in the available studies. The principal effect of p-chloro-m-cresol toxicity was a slight reduction in body weight gain. It was concluded that an increase in dosing duration did not result in increased toxicity, reflected by comparable No Observed Effect Levels (NOELs) in rats following 3-month and 2-year periods of dietary administration of p-chloro-m-cresol. The lowest NOEL (30 mg/kg bw/day) for p-chloro-m-cresol effects on body weight gains was reported in a gavage developmental study in rats. p-Chloro-m-cresol was not teratogenic when tested up to 300 mg/kg bw/day in rats. Although a reproduction study was not submitted for this active ingredient; the results of a 2-year oral rat study did not reveal any adverse effects on reproductive organs through histopathological examination or demonstrate carcinogenic potential.

Based on the registered use pattern for p-chloro-m-cresol and sodium p-chloro-m-cresolate, exposure of workers is expected to be intermittent over an intermediate- to long-term duration and primarily via the dermal route. Dietary exposure was not expected based on the registered use pattern.

The NOEL of 160 mg/kg bw/day from the 21-day dermal toxicity study in the rat was considered by the PMRA to be the most appropriate endpoint for assessment of dermal exposure at the time of the initial registration. Although the use of these pesticides in industrial settings spans more than a 21-day period, considering that in the available toxicological studies no increase in toxicity was observed with an increase in dosing duration, characterizing risk based on the selected NOEL from a 21-day dermal toxicity study was not expected to underestimate the potential dermal risk. Standard uncertainty factors of 10-fold for interspecies extrapolation and a 10-fold for intraspecies variations have been applied resulting in a target margin of exposure (MOE) of 100.

The maternal NOEL of 30 mg/kg bw/day from the rat gavage developmental toxicity study was lower than the selected dermal endpoint. However, considering that the rat developmental study employed bolus administration of p-chloro-m-cresol which is not representative of the expected route of exposure based on the registered use pattern and, the critical effects on the dams were general in nature and have been examined in a dermal toxicity study, the PMRA concluded that

characterizing risk based on a dermal endpoint is not expected to underestimate the human health risk. With respect to potential effects of p-chloro-m-cresol on the young, the available data showed no effects of concerns.

Appendix II lists toxicicological endpoints used by the PMRA for human health risk assessment.

3.2 Occupational Exposure

Exposure to p-chloro-m-cresol and sodium p-chloro-m-cresolate may occur while mixing/loading the pesticide in industrial settings and through contact with treated materials/products.

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a MOE. This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive population subgroup. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

3.2.1 Chemical Handler Exposure and Risk

In industrial settings, workers can apply the commercial end-use product containing p-chloro-m-cresol and sodium p-chloro-m-cresolate to materials or solutions to be preserved using open or closed system technology. Based on the current use pattern for p-chloro-m-cresol and sodium p-chloro-m-cresolate, exposure of workers is expected to be intermittent over an intermediate- to long-term duration and predominantly via a dermal route.

The occupational dermal exposure and risk assessment for primary chemical handlers was conducted by the PMRA at the time of the initial registration using the 90th percentile of the exposure estimate derived from the Chemical Manufacturers Association (CMA) Antimicrobial Exposure Study for workers applying solid (mostly powder) formulations. The estimated dermal MOE was 145 and not of concern (target MOE of 100). Based on a high vapour pressure of this active ingredient, there is a concern for inhalation exposure of workers applying the antimicrobial products via open pouring. Using the 90th percentile of the inhalation exposure dose from the CMA study and the lowest oral NOEL reported in the p-chloro-m-cresol toxicological database, the estimated MOE was above 16000. On this basis, the PMRA concluded that inhalation exposure of workers applying p-chloro-m-cresol and sodium p-chloro-m-cresolate via open pouring is unlikely to result in a risk of concern.

The occupational assessment based on the exposure estimate for workers handling a powder formulation is considered highly conservative and encompasses potential exposures resulting from mixing/transfer of flake or liquid formulations.

Based on severe eye and skin irritation properties of the commercial end-use product containing p-chloro-m-cresol, the PMRA proposes additional personal protective equipment (PPE) for all workers during handling, clean up, and repair activities. The proposed label amendments are listed in Appendix III.

3.2.2 Postapplication Exposure and Risk

Following the application of p-chloro-m-cresol and sodium p-chloro-m-cresolate in industrial settings, workers can be exposed to these active ingredients while coming in contact with treated materials/products (for example, metalworking fluids).

Based on the currently registered use pattern for p-chloro-m-cresol and sodium p-chloro-m-cresolate, the PMRA identified three scenarios representing the highest potential for postapplication occupational exposure:

- Industrial/manufacturing bystanders
- Workers exposed to treated metalworking fluids
- Workers exposed to treated materials/products (for example, adhesives, joints cements)

Industrial/manufacturing bystander
Postapplication exposure of workers in industrial settings following applications of p-chloro-m-cresol and sodium p-chloro-m-cresolate to open vats of liquids such as adhesives, coating, paints, or emulsions was expected to be minimal considering a limited dermal contact with treated solution and the degree of dilution of the applied end-use products in treated liquids.

Workers exposed to treated metalworking fluids
For workers exposed to metalworking fluids treated with p-chloro-m-cresol or sodium p-chloro-m-cresolate, both inhalation and dermal exposures are expected. Considering a significant dilution of these active ingredients in treated metal working fluids, exposure of workers to these active ingredients is considered by the PMRA to be lower than exposure of primary handlers applying concentrated end-use products using open system technology. Given that the results of the risk assessment for primary handlers indicated no risks of concern and PPE currently required on the registered product labels, exposure of workers to p-chloro-m-cresol and sodium p-chloro-m-cresolate in treated metalworking fluids is considered unlikely to result in a risk of concern.

Workers exposed to treated materials/products
For workers exposed to finished product containing p-chloro-m-cresol or sodium p-chloro-m-cresolate, exposures to treated paints represents the worst case scenario considering the amount of active ingredient handled per day. An assessment of a professional painter exposure was conducted during the re-evaluation using the unit exposure value from the Pesticide Handlers Exposure Database for a worker wearing a single layer clothing and no gloves, assuming the maximum Canadian application rate in paint of 0.4% and a typical volume of paint applied of 19 L and 190 L for a paintbrush and airless sprayer scenario, respectively (based on the previous PMRA assessment for similar antimicrobial active ingredients). The estimated dermal MOEs were above 174 and not of concern (target MOE of 100). Using the lowest oral NOEL reported in the p-chloro-m-cresol toxicological database, the estimated inhalation MOEs were above 2500. On this basis, the PMRA concluded that that inhalation exposure of professional painters is unlikely to result in a risk of concern.

No further mitigation measures are proposed for postapplication workers.

3.3 Non-Occupational Exposure

Currently there are no end-use products containing p-chloro-m-cresol or sodium p-chloro-m-cresolate intended for residential use, therefore, any exposures in these settings would be limited to those involving exposure to residues in finished products.

3.3.1 Residential Exposure and Risk

Considering the low toxicity of the technical grade p-chloro-m-cresol, the dilution of p-chloro-m-cresol and sodium p-chloro-m-cresolate during the manufacturing process, and infrequent use of these products by homeowners, potential postapplication residential exposures are considered unlikely to result in risks of concern. No further mitigation measures are proposed.

3.3.2 Residue Limits in Food Commodities

As there are no food or feed crops uses registered for p-chloro-m-cresol and sodium p-chloro-m-cresolate in Canada, no Maximum Residue Limits have been established.

3.3.3 Dietary Exposure and Risk

Dietary exposure to p-chloro-m-cresol and sodium p-chloro-m-cresolate is not expected because these active ingredients are not registered for use on food or feed crops. Further, the current commercial end-use product labels prohibit the use of these active ingredients in materials intended for food contact. Exposure from drinking water is not expected based on the current use pattern and a rapid degradation in water. Consequently, a dietary exposure and risk assessment was not required.

3.3.4 Aggregate Exposure and Risk

Aggregate risk combines the different routes of exposure to p-chloro-m-cresol and sodium p-chloro-m-cresolate. Short-term and intermediate-term aggregate risk assessments are comprised of contributions from food, drinking water and non-occupational exposure (dermal and/or inhalation).

Given that dietary and drinking water exposures are not expected and the co-occurrence of residential exposure is unlikely based on the extent of use of these pesticides, an aggregate risk assessment for p-chloro-m-cresol and sodium p-chloro-m-cresolate was not required.

3.3.5 Cumulative Exposure and Risk

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with common mechanism of toxicity. The PMRA has not yet determined whether p-chloro-m-cresol and sodium p-chloro-m-cresolate have a common mechanism of toxicity with other compounds, consequently a cumulative assessment was not conducted during the re-evaluation review.

4.0 Environment

4.1 Environmental Fate

The environmental fate and risk assessment was conducted by the PMRA at the time of the original registration. The submitted data indicated that p-chloro-m-cresol has a low potential for leaching and that it biotransforms in soil. An analysis of wastewater indicated that primary anaerobic treatment resulted in reduction of p-chloro-m-cresol in wastewater and that, after secondary aerobic treatment no p-chloro-m-cresol was detected.

Bioaccumulation was considered unlikely based on the octanol-water partition coefficient factor of 3.02 and 2.86 reported[3] for p-chloro-m-cresol and sodium p-chloro-m-cresolate, respectively.

4.2 Environmental Exposure and Risk Assessment

At the time of the original registration, the PMRA determined that the use of p-chloro-m-cresol and sodium p-chloro-m-cresolate as material preservatives in industrial settings was of low environmental concern based on the low probability of exposure to the environment and a rapid degradation of p-chloro-m-cresol in water.

Given the currently registered use pattern for p-chloro-m-cresol and sodium p-chloro-m-cresolate in Canada, the PMRA concluded that p-chloro-m-cresol and sodium p-chloro-m-cresolate are unlikely to cause harm to the environment. No additional data is required.

Based on current PMRA practices, standard advisory label statements to minimize surface water contamination and for storage are proposed to be included on the commercial end-use product label. The proposed label amendments are listed in Appendix III.

5.0 Value

p-Chloro-m-cresol and sodium p-chloro-m-cresolate have a wide spectrum of activity and provide additional active ingredients for use as material preservatives.

[3] 2011 USEPA *Summary of Product Chemistry, Environmental Fate, and Ecotoxicity Data for the p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Registration Review Decision Document*; Docket No. EPA-HQ-OPP-2011-0073

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, for example, persistent (in air, soil, water and/or sediment), bioaccumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the re-evaluation process, p-chloro-m-cresol and sodium p-chloro-m-cresolate were assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy,* and evaluated against the Track 1 criteria. In order for p-chloro-m-cresol and sodium p-chloro-m-cresolate to meet Track 1 criteria, the criteria for both bioaccumulation and persistence (in one media) must be met. The PMRA has reached the following conclusion:

- Persistence: p-Chloro-m-cresol half-life in soil ranges from 1.4 to 21 days. Given that TSMP Track 1 criterion is a half-life in soil or water ≥182 days or in sediment >365 days it is concluded that p-chloro-m-cresol does meet the criteria for persistence.
- Bioaccumulation: The octanol-water partition coefficient factor of 3.02 for p-chloro-m-cresol and, of 2.86 for sodium p-chloro-m-cresolate was reported. Given that TSMP Track 1 criterion is ≥5.0 it is concluded that p-chloro-m-cresol and sodium p-chloro-m-cresolate do not meet the criteria for bioaccumulation.
- p-Chloro-m-cresol and sodium p-chloro-m-cresolate do not meet all Track 1 criteria and therefore are not considered Track 1 substances.

6.2. Contaminants and Formulants of Health or Environmental Concern

During the re-evaluation of p-chloro-m-cresol and sodium p-chloro-m-cresolate, contaminants in the technical are compared against the *List of Pest control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[4]. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including DIR99-03 and DIR2006-02, 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 conclusion:

- Technical grade p-chloro-m-cresol and sodium p-chloro-m-cresolate do not contain any contaminants of health or environmental concern identified in the *Canada Gazette.*

[4] *Canada Gazette*, Part II, Volume 139, Number 24, 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, 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.*

The use of formulants in registered pest control products is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

During the review process, the potential presence of impurities known to have, or suspected to have, health and/or environmental implications are assessed in accordance with DIR98-04.[5] Based on the manufacturing process, impurities of human health or environmental concern, including TSMP Track 1 substances, are not expected to be present in the p-chloro-m-cresol and sodium p-chloro-m-cresolate products.

7.0 Incident Reports

Since 26 April 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. Registrants must also provide a scientific study they have sponsored if it indicates a new health or environmental hazard, increased health or environmental risk or the presence of a component or derivative that has not been previously detected.

As of 19 March 2013 no reports of incidents have been reported to the PMRA for p-chloro-m-cresol or sodium p-chloro-m-cresolate.

8.0 Organisation for Economic Co-operation and Development Status

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups 34 member countries and provides governments with a setting in which to discuss, develop and perfect economic and social policies.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

p-Chloro-m-cresol and sodium p-chloro-m-cresolate are currently acceptable for use in several OECD countries, including the United States.

The European Commission implemented decisions in 2008 and 2010 prohibiting the use of p-chloro-m-cresol and sodium p-chloro-m-cresolate in certain biocidal product types. However, the European Commission decision was due to withdrawn or incomplete support for these chemicals in the European review program and was not as a result of a health or environmental concern.

No decision by an OECD member country to prohibit all uses of p-chloro-m-cresol or sodium – chloro-m-cresolate for health or environmental reasons has been identified.

[5] DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product.*

9.0 Proposed Re-evaluation Decision

The PMRA has determined that products containing p-chloro-m-cresol and sodium p-chloro-m-cresolate for sale and use in Canada 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 product must be amended to include the label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. No additional data are being required at this time.

10.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2012-02, *Re-evaluation Program Cyclical Re-evaluation*, and DACO tables can be found on the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra.infoserv@hc-sc.gc.ca.

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

List of Abbreviations

°C	degree(s) Celsius
λ	wavelength(s)
bw	body weight
CAS	Chemical Abstracts Service
CMA	Chemical Manufacturers Association
DACO	data code
g	gram(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
L	litre(s)
mg	milligram(s)
MOE	margin of exposure
nm	nanometre
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
Pa	Pascal
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
PRVD	Proposed Re-evaluation Decision
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Registered p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate Products as of 17 July 2013

Table 1 p-Chloro-m-cresolate Products

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (w/w)
25512	Technical	LANXESS CORPORATION	Preventol CMK	Pellet	99.8%
28818	Commercial	LANXESS CORPORATION	PREVENTOL CMK PRESERVATIVE	Pellet	99.8%

Table 2 Sodium p-Chloro-m-cresolate Products

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (w/w)
25513	Technical	LANXESS CORPORATION	PREVENTOL CMK-NA	Flakes	99.4%
27426	Commercial	LANXESS CORPORATION	PREVENTOL CMK 40	Solution	40%*
28308	Commercial	LANXESS CORPORATION	PREVENTOL CMK-NA PRESERVATIVE	Flakes	99.4%

* Calculated as p-chloro-m-cresol

Appendix II Toxicological Endpoint for p-Chloro-m-cresol Human Health Risk

Exposure Scenario	Dose (mg/kg bw/day)	Study	Target MOE
Dermal exposure	NOEL = 160	21-day dermal exposure study in rabbits, no systemic effects observed at the highest dose tested.	100
Inhalation exposure	NOEL = 30	Gavage developmental exposure study in rats, effects on body weight gains in dams at a LOEL of 100 mg/kg bw/day	100

NOEL = no observed effect level

Appendix III Label Amendments for Products Containing p-Chloro-m-cresol and Sodium p-Chloro-m-cresolate

The label amendments presented below 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 following label statements.

The following label statements to further protect human health and the environment are proposed to be included on the commercial end-use product label.

I) The following statements are proposed to be included in the section entitled **PRECAUTIONS**.

> Wear protective eyewear (goggles or face shield), chemical-resistant coveralls over long-sleeved shirt and long pants, and chemical-resistant gloves and footwear during handling, clean up, and repair activities, and when handling treated metalworking fluid concentrates.

II) The following statements are proposed to be included in the section entitles **DIRECTIONS FOR USE**

> **DO NOT** contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes.
>
> **DO NOT** discharge effluents containing this product into sewer systems, lakes, streams, ponds, estuaries, oceans, and other waters.

References

A. Information Considered in the Chemistry Assessment

Studies/Information Submitted by Applicant/Registrant (Unpublished)

PMRA Document Number	Reference
1856794	1991, PVJ-BBA-1 Preventol CMK Product Identity, Manufacturer Method, Specification, Quality Control, Analytical Data and Methodology, Chemical and Physical Properties, MSDS, DACO:0.9,2.1,2.10,2.11,2.12,2.13,2.14,2.15, 2.2,2.3,2.4,2.5,2.6,2.7,2.8,2.9
1465836	1991, Technical Chemistry file - PVK-BBA-9. Preventol CMK Na. Basic Chemistry information, Manufacturing Method, Specifications, Volumetric Method, Titer-Volumetric Method, UV Spectrum, MSDS, DACO: 2.1,2.10,2.11,2.12,2.13,2.14,2.15,2.16,2.2,2.3,2.4,2.5,2.

B. Information Considered in the Human Health Risk Assessment

Studies/Information Submitted by Applicant/Registrant (Unpublished)

PMRA Document Number	Reference
1136007	1989, Range-Finding Subacute Toxicological Investigations in Wistar Rats for the Determination of a Maximum Tolerable Dosage, Part 2 of 2, DACO: 4.3.1
1139190	1993, Preventol CMK Chronic Toxicity and Carcinogenicity Study in Wistar Rats, DACO: 4.4.1
1145456	1981, Acute Oral Toxicity of PCMC (P-Chlor-M-Cresol) to Rats, DACO: 4.2.1
1145457	1988, Investigation of Acute Cutaneous Toxicity in Male and Female Wistar Rats, DACO: 4.2.2
1145458	1979, Acute Dermal Administration Study in Male and Female Rabbits, DACO: 4.2.2
1145459	Investigation of Skin and Mucous Membrane Tolerance/Irritant Effect on Skin and Mucous Membrane-Individual Results (Preventol CMK), DACO: 4.2.4,4.2.5

1145460 1981, Study for Acute Toxicity of Fumes and Dusts after Inhalation -Rats, DACO: 4.2.3

1145464 1981, Evaluation to Determine the Sensitization Effect by Means of the Open Epicutaneous Test Guinea Pigs, DACO: 4.2.6

1145465 1980, Investigation of Sensitizing Effect -Guinea Pigs, DACO: 4.2.6

1145469 1989, Range-Finding Subacute Toxicological Investigations in Wistar Rats for the Determination of a Maximum Tolerable Dosage, Part 1 of 2, DACO: 4.3.1

1145470 1980, Subchronic Dermal Study in Rabbits Revised Final Report, DACO: 4.3.4

1145471 1988, Subchronic Toxicological Study in Rats, DACO: 4.3.1

1145473 1990, Preventol CMK-Chronic Study Combined with Oncogenicity, DACO: 4.4.1

1145476 1993, Chronic Toxicity and Carcinogenicity Study in Wistar Rats, DACO: 4.4.1

1145478 1991, Embryotoxicity (Including Teratogenicity) Study in Rats with Preventol CMK after Oral Administration, DACO: 4.5.2

1145480 1991, Study for Embryotoxic Effects in Rats after Oral Administration, DACO: 4.5.2

1145481 1980, Salmonella/Microsome Test for Detection Of Point Mutagenic Effects, DACO: 4.5.4

1145482 1986, 4-Chloro-3methylphenol: Salmonellla/Mammalian-Microsome Mutagenicity Test plus Subacute Toxicity Test in Rats, DACO: 4.5.4

1145483 1989, Mutagenicity Study for the Detection of Induced Forward Mutations in the CHO-HGPRT Assay In Vitro, DACO: 4.5.4

1145484 1988, Mutagenicity Test on Preventol CMK in the Rat Primary Hepatocyte Unscheduled DNA Synthesis Assay, DACO: 4.5.4

1145485 1990, Micronucleus Test In Vivo in Mice on the Chromosome of the Erhtroblastes of the Bone Marrow, DACO: 4.5.4

1166486 Chronic Toxicity and Caricinogenicity Study in Wistar Rats. Supplement: Historical Data on the Incidence of Pituitary Gland (Pars Distalis) and Leydig Cell Tumors, DACO: 4.4.4

1145506 Chemical Manufacturers Association Antimicrobial Exposure Assessment Study (Q626)(Preventol CMK), DACO: 5.1

C. Information Considered in the Environmental Risk Assessment

Studies/Information Submitted by Applicant/Registrant (Unpublished)

PMRA Document Number	Reference
1166489	Preventol CMK, CMK-Na: Analysis of Wastewater from the Leather Industry, DACO: 8.3.4

Additional Information Considered

Published Information

1162827	Detecting Organic Contaminants in the Unsaturated Zone Using Soil and Soil-Pore Water Samples (K.W. Brown,G.C. Barbee,J.C. Thomas And H.E. Murray; Hazardous Waste & Hazardous Materials, Vol. 7 No. 2, 1990: 151-168 (Preventol CMK), DACO: 8.2.3.4.2
1162828	Loss of Organic Chemicals in Soil: Pure Compound Treatability Studies (R.C. Loehr & J.E. Matthews; Journal of Soil Contamination, 1(4): 339-360)(Preventol CMK), DACO: 8.2.3.4.2
1162829	Fate of Chlorinated Cresols from Environmental Samples (M.A Sattar; Chemosphere, Vol.19 Nos. 8/9: 1421-1426 (1989))(Preventol CMK), DACO: 8.2.3.4.2