Proposed Registration Decision PRD2024-08

Copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles

(*publié aussi en français*)

28 November 2024

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

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Canada

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

Catalogue number: H113-9/2024-8E (print version)
H113-9/2024-8E-PDF (PDF version)

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Overview

Proposed registration decision for copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles

Health Canada's Pest Management Regulatory Agency (PMRA), pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Cupric Oxide, containing the active ingredient copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles containing the active ingredient copper (present as cuprous oxide), as an in-can and dry-film preservative against bacteria and yeast.

In addition, Corning Guardiant Antimicrobial Particles may also be used to formulate paints and coatings registered under the *Pest Control Products Act* that have residual antimicrobial effectiveness after application to indoor hard surfaces (kills 99.9% of bacteria and viruses within two hours on painted surfaces). All formulators wanting to use Corning Guardiant Antimicrobial Particles for residual indoor hard surface efficacy are responsible for registering their pesticide products under the *Pest Control Products Act*.

The active ingredient copper is present as cupric oxide in the technical grade active ingredient and is converted to cuprous oxide in Corning Guardiant Antimicrobial Particles.

Copper (present as cupric oxide and cuprous oxide) containing pesticides are currently registered as broad spectrum fungicides, bactericides and antifouling agents for use in antifouling paints, sanitizers, material preservatives, and wood preservatives. For details, see the Proposed Re-evaluation Decision, PRVD2009-04, *Copper Pesticides*, and the Re-evaluation Decision, RVD2010-05, *Copper Pesticides*.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles.

What does Health Canada consider when making a registration decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to individuals and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed

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

conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children). They also consider the unique characteristics of organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how Health Canada regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Canada.ca website.

Before making a final registration decision on copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles, Health Canada's PMRA will consider any written comments received from the public in response to this consultation document.[3] Health Canada will then publish a Registration Decision[4] on copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and Health Canada's response to these comments.

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

What is copper (present as cupric oxide or cuprous oxide)?

Copper has well-known antimicrobial properties. Copper ions can kill bacteria and viruses by destroying lipid membranes, protein coats, and cell membranes using multiple mechanisms of action. This renders the structures of microorganisms non-functional.

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

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

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

Health considerations

Can approved uses of copper (present as cupric oxide or cuprous oxide) affect human health?

Copper (present as cupric oxide or cuprous oxide) is unlikely to affect human health when used according to label directions.

The active ingredient copper is present as cupric oxide in the technical grade active ingredient and is converted to cuprous oxide in the end-use product.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. 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 levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effect in animal testing are considered acceptable for registration.

Potential exposure to copper (present as cupric oxide or cuprous oxide) may occur when handling the product. In laboratory animals, copper (present as cupric oxide) was of low acute toxicity via the oral, dermal and inhalation routes, moderately irritating to the eye, mildly irritating to the skin and not a dermal sensitizer.

Copper is a naturally-occurring metal that is present in many foods and in drinking water. Copper is also an essential element in maintaining normal health in humans, with adverse effects more likely to result from copper deficiency rather than excess.

There was no evidence of copper being carcinogenic or resulting in any other systemic toxicity in animals having normal copper homoeostasis. Available studies in animals generally indicate that the main concern for reproductive and developmental effects is associated with copper deficiency rather than excess.

Copper, present as cuprous oxide, is characterized as being of low acute toxicity by the oral and dermal routes, highly toxic by the inhalation route, severely irritating to the eyes and skin, and not a dermal sensitizer.

The end-use product, Corning Guardiant Antimicrobial Particles, containing copper (present as cuprous oxide), is of slight acute toxicity by the oral route, low acute toxicity by the dermal and inhalation routes, mildly irritating to the eyes, non-irritating to the skin and not a dermal sensitizer.

Residues in water and food

Dietary risks from food and water are acceptable.

The end-use product, Corning Guardiant Antimicrobial Particles, is not proposed for food or feed uses. Dietary or drinking water exposure is not expected from the proposed use of copper (present as cuprous oxide) as a material preservative. Consequently, health risks from dietary exposure are acceptable for all segments of the population, including infants, children, adults and seniors.

Risks in residential and other non-occupational environments

Estimated risk for residential and other non-occupational exposure is acceptable.

Corning Guardiant Antimicrobial Particles will only be added to paints in paint manufacturing facilities. Consequently, the health risk to residents and the general public is acceptable.

Paint containing Corning Guardiant Antimicrobial Particles as an in-can preservative will be used by both professional and residential painters. Standard mitigating statements are required on paints sold in Canada.

Occupational risks from handling Corning Guardiant Antimicrobial Particles

Occupational risks are acceptable when Corning Guardiant Antimicrobial Particles is used according to the label directions, which include protective measures.

Workers handling Corning Guardiant Antimicrobial Particles can come into direct contact with copper (present as cuprous oxide) through contact with the skin or by inhalation during loading, clean-up and repair.

To protect workers from exposure to the end-use product, the label requires workers to wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during loading, clean-up and repair. Precautionary and hygiene statements on the label are considered adequate to protect individuals from occupational exposure.

The health risks to workers are acceptable when the precautionary statements on the label are observed.

Environmental considerations

An environmental assessment was not required given that the proposed major new uses for copper (present as cupric oxide) and its associated end-use product, Corning Guardiant Antimicrobial Particles (containing copper present as cuprous oxide), are only for indoor use.

Value considerations

What is the value of Corning Guardiant Antimicrobial Particles?

Corning Guardiant Antimicrobial Particles contain copper (present as cuprous oxide), which can be used to inhibit the in-can and dry-film growth of bacteria and yeast, and can kill 99.9% of bacteria and viruses on coated surfaces within two hours of exposure.

The registration of the Corning Guardiant Antimicrobial Particles, containing 27% copper present as cuprous oxide, will offer a novel in-can and dry-film preservative for use in paints, protecting against bacteria and yeast.

For use in formulating paint and coatings registered under the *Pest Control Products Act* that have residual antimicrobial effectiveness after application to indoor hard surfaces (kills 99.9% of bacteria and viruses within two hours on painted surfaces), Corning Guardiant Antimicrobial Particles would be applied at a rate of 52–100 g/3.78 L of paint. All formulators wanting to use Corning Guardiant Antimicrobial Particles for indoor hard surface efficacy are responsible for registering their pesticide products under the *Pest Control Products Act*.

Measures to minimize risk

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

The key risk-reduction measures being proposed on the label of Cupric Oxide and Corning Guardiant Antimicrobial Particles to address the potential risks identified in this assessment are as follows.

Key risk-reduction measures

Human health

The hazard signal words “WARNING – EYE IRRITANT” and “CAUTION – SKIN IRRITANT” are required on the principal display panel for Cupric Oxide and “CAUTION POISON” and “CAUTION – EYE IRRITANT” are required on the principal display panel for Corning Guardiant Antimicrobial Particles. Standard precautionary statements are also required on the labels to inform users that the TGAI causes eye and skin irritation and that the EP is harmful if swallowed, and causes eye irritation.

Workers are required to wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during loading, clean-up and repair.

To limit bystander exposure, the end-use product label requires a statement indicating only authorized access is permitted in the area during handling.

Environment

The Corning Guardiant Antimicrobial Particles label will require a statement ‘toxic to aquatic organisms’, due to the inherent toxicity of copper and ‘FOR INDOOR USE ONLY’ will be added to the primary panel.

Next steps

Before making a final registration decision on copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles, Health Canada’s PMRA will consider any written comments received from the public in response to this consultation document up to 45 days from the date of publication (28 November 2024) of this document. Please forward all comments to PMRA Publications, through the Public Engagement Portal (Public Engagement Forms – Consultation Comment). Health Canada will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed decision and Health Canada’s response to these comments.

Other information

When Health Canada makes its registration decision, it will publish a Registration Decision on copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles (based on the

Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA’s Reading Room. For more information or if you have questions, please contact the PMRA’s Pest Management Information Service.

Science evaluation

Copper, present as cupric oxide, and Corning Guardiant Antimicrobial Particles

1.0 The active ingredient, its properties and uses

1.1 Identity of the active ingredient

Active substance	Copper, present as cupric oxide
Function	Heavy duty wood preservative, sanitizer
Chemical name	
1. International Union of Pure and Applied Chemistry (IUPAC)	Copper(II) oxide
2. Chemical Abstracts Service (CAS)	Copper oxide (CuO)
CAS number	1317-38-0
Molecular formula	CuO
Molecular weight	79.55
Structural formula	$Cu^{2+}O^{2-}$
Purity of the active ingredient	78.8 %

1.2 Physical and chemical properties of the active ingredient and end-use product

Technical product—Cupric Oxide

Property	Result
Colour and physical state	Black/dark gray powder
Odour	Odourless
Melting range	1025°C
Boiling point or range	Not applicable
Density	Bulk density at 20°C: 6.32 g/cm^3
Vapour pressure at 20 °C	Not applicable
Ultraviolet (UV)-visible spectrum	Waived because of low solubility

Property	Result
Solubility in water	0.729 mg/L
Solubility in organic solvents at 20°C	Solvent Solubility mg/L) acetone 0.296
n–Octanol-water partition coefficient (K_{ow})	Not required
Dissociation constant (pK_a)	Not required
Stability (temperature, metal)	Stable at < 1000°C No reaction with Cu, Zn or stainless steel

End-use product—Corning Guardiant Antimicrobial Particles

Property	Result
Colour	Orange
Odour	Odourless
Physical state	Solid
Formulation type	Solid
Label concentration	Copper, present as cuprous oxide at 27%
Container material and description	HDPE Nalgene Plastic Bottles LDPE Lined Paper Bags LDPE Plastic Lined Fiber Drums
Density	2.866 g/cm^3 at 25°C
pH of 1% dispersion in water	8.777
Oxidizing or reducing action	The product does not contain a strong oxidizing or reducing agent.
Storage stability	The active was found to be stable when the product is stored in the commercial HDPE container for 2 weeks at 54°C.
Corrosion characteristics	With the exception of a slight colour change, no adverse effects were noted to the commercial HDPE container over 2 weeks storage at 54°C.
Explodability	The product does not have explosive properties.

1.3 Directions for use

Corning Guardiant Antimicrobial Particles

Corning Guardiant Antimicrobial particles consist of a glass microstructure which stores copper (present as cuprous oxide), allowing for a slow controlled release of copper ions. When incorporated into paints, it can be used as an in-can and dry-film preservative to prevent spoiling due to bacteria and yeast. An in-can preservative inhibits the growth of spoilage organisms such as bacteria and yeast during the storage of materials such as solutions, dispersions, and

emulsions, while a dry-film preservative inhibits the spoilage and discolouration of the film once applied and dried. It can also be used to formulate paint, which requires registration, that demonstrate supplemental residual efficacy (99.9% reduction within 2 hours) against bacteria and viruses when applied to a surface.

The product is to be used as an in-can preservative for paints to prevent spoiling from bacteria and yeast at a rate of 1−5 grams per 3.78 L of paint. This product can also be used to formulate registered paints and coatings that have residual effectiveness on indoor hard surfaces against viruses and bacteria (kills 99.9% of bacteria and viruses within two hours on painted surfaces), with a use rate of 52−100 grams per 3.78 L of paint.

1.4 Mode of action

Copper is well known to have antimicrobial properties. The glass microstructure stores copper (present as cuprous oxide), allowing for a slow controlled release.

The controlled, steady release of copper ions in the painted surface allows for contact killing of bacteria and viruses present and thus provides residual effectiveness against viruses and bacteria on treated surfaces. Using multiple mechanisms of action, the copper acts against the cell membrane, proteins, DNA, and RNA. By destroying key structures of microorganisms, the copper ions can render the microorganisms non-functional.

2.0 Methods of analysis

2.1 Methods for analysis of the active ingredient

Not required for this application as they were previously reviewed and assessed to be acceptable.

2.2 Method for formulation analysis

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

2.3 Methods for residue analysis

No methods are required to quantify residues of copper as there is no proposed food use (see Section 3.2.1 for additional details).

3.0 Impact on human and animal health

3.1 Toxicology summary

The active in the technical grade active ingredient is in the form of copper (present as cupric oxide). The copper in the technical grade active ingredient is reduced to copper (present as cuprous oxide) in the end-use product. A detailed review of toxicology information was

conducted in support of the technical grade active ingredient, Cupric Oxide, and the end-use product, Corning Guardiant Antimicrobial Particles. The data package for Cupric Oxide and Corning Guardiant Antimicrobial Particles, is considered acceptable to assess the toxic effects that may result from exposure to copper.

As per the Proposed Re-evaluation Decision PRVD2009-04, *Copper Pesticides*, copper (present as cupric oxide) is of low acute toxicity via the oral, dermal and inhalation routes, moderately irritating to the eye, mildly irritating to the skin, and not a dermal sensitizer. The component of toxicological interest in copper-containing pesticides is elemental copper (cupric ion). Humans have homeostatic capabilities to regulate copper. There is no evidence of copper being carcinogenic or posing any other systemic toxicity in animals having normal copper homeostasis. Thus, toxicological endpoints were not established to quantify any potential risks from exposure to copper. Refer to the Proposed Re-evaluation Decision, PRVD2009-04, *Copper Pesticides* for additional details.

The toxicology profile of copper, present as cuprous oxide, is characterized as being of low acute toxicity by the oral and dermal routes, highly toxic by the inhalation route, severely irritating to the eyes and skin, and not a dermal sensitizer. Refer to the Proposed Re-evaluation Decision, PRVD2009-04, *Copper Pesticides* for additional details.

The data package for Corning Guardiant Antimicrobial Particles consisted of acute toxicity studies (acute oral, dermal and inhalation toxicity, eye and skin irritation, and dermal sensitization). Corning Guardiant Antimicrobial Particles (copper, present as cuprous oxide) is considered to be of slight acute toxicity by the oral route, low acute toxicity by the dermal and inhalation routes, mildly irritating to the eyes, non-irritating to the skin and not a dermal sensitizer.

3.2 Occupational, residential and bystander exposure and risk assessment

3.2.1 Use description

Corning Guardiant Antimicrobial Particles is proposed for use as an in-can and dry-film preservative for paints to prevent spoiling from bacteria and yeast. The end-use product will be added to paints manufactured in paint facilities, and the treated paints are proposed for use by both professional and residential painters.

For use as an in-can preservative for paints to prevent spoiling from bacteria and yeast, Corning Guardiant Antimicrobial Particles is applied at a rate of 1–5 grams per 3.78 L of paint.

For use in formulating paints and coatings registered under the *Pest Control Products Act* that have residual indoor hard surface efficacy against viruses and bacteria (kills 99.9% of bacteria and viruses within two hours on painted surfaces), Corning Guardiant Antimicrobial Particles would be applied at a rate of 52–100 g/3.78 L of paint. All formulators wanting to use Corning Guardiant Antimicrobial Particles for residual indoor hard surface efficacy are responsible for registering their pesticide products under the *Pest Control Products Act*.

3.2.2 Occupational exposure and risk assessment

3.2.2.1 Mixer, loader, and applicator exposure and risk assessment

When handled according to label instructions, occupational exposure to Corning Guardiant Antimicrobial Particles is characterized as short- to intermediate-term in duration and is expected to occur by the dermal and inhalation routes during loading, clean-up and repair. To protect workers from exposure to Corning Guardiant Antimicrobial Particles, workers are required to wear a long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes during loading, clean-up and repair. Precautionary statements on the end-use product labels aimed at mitigating exposure are adequate to protect individuals from any risk due to occupational exposure. Overall, health risks to workers are acceptable when the precautionary statements on the labels are followed which include personal protective equipment (PPE).

3.2.2.2 Postapplication exposure and risk assessment

Postapplication activities include typical activities related to packaging and distributing paints. Precautionary statements on the end-use product labels aimed at mitigating exposure are adequate to protect workers from risk due to post-application exposure. Consequently, the health risks to workers due to post-application exposure are acceptable.

3.2.3 Residential and bystander exposure and risk assessment

Bystander exposure is not expected to be of concern from the use of Corning Guardiant Antimicrobial Particles. Due to the automated systems used in paint manufacturing facilities, bystander exposure to Corning Guardiant Antimicrobial Particles is not expected to occur. Additionally, only workers wearing PPE may be in the area during loading, clean-up and repair.

Paints containing Corning Guardiant Antimicrobial Particles as an in-can preservative will be used by both professional and residential painters. Paints treated with an antimicrobial preservative (in-can preservative) do not require registration if the pesticide treating the article is registered under the *Pest Control Products Act*. Refer to Health Canada's Information Note - Treated Articles 1 September 2022 for additional details. Standard mitigating statements are required on paints sold in Canada to protect professional and residential painters.

Consequently, the health risks to bystanders and individuals in residential areas are considered acceptable.

3.3 Dietary exposure risk assessment

3.3.1 Food

Corning Guardiant Antimicrobial Particles is not proposed for food or feed use. Consequently, dietary exposure to copper (present as cuprous oxide) from the proposed use is not of concern and a dietary risk assessment is not required.

3.3.2 Drinking water

Based on the proposed use pattern (see Section 3.2.1), exposure from drinking water is not expected. The label has the necessary mitigative measures to prevent contamination of drinking water from the proposed use of copper (present as cupric or cuprous oxide). Additionally, copper is a naturally occurring metal that occurs in many foods and in drinking water. Consequently, health risks from residues of copper (present as cupric or cuprous oxide) in drinking water are acceptable.

3.3.3 Acute and chronic dietary risks for sensitive subpopulations

As noted above, when the end-use product is used as directed by the label, the health risk is acceptable for the general population, including infants and children, and domestic animals.

3.4 Aggregate exposure and risk

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources, and from all known or plausible exposure routes (oral, dermal and inhalation).

In an aggregate risk assessment, the combined potential risk associated with food, drinking water and various residential exposure pathways is assessed. A major consideration is the likelihood of co-occurrence of exposures. Additionally, only exposures from routes that share common toxicological endpoints can be aggregated.

Cupric oxide is considered to be of low toxicity by the oral, dermal, and inhalation routes, and cuprous oxide is considered to be of low acute toxicity by the oral and dermal routes and highly toxic by the inhalation route. The end-use product is not proposed for food use and will not be applied near, or to, drinking water. Furthermore, non-occupational exposure will be low when Corning Guardiant Antimicrobial Particles is used as directed on the label. When the end-use product is used as labelled, there is reasonable certainty that no harm will result from aggregate exposure of residues of cuprous oxide. This includes all anticipated dietary (food and drinking water) exposures and all other non-occupational exposures (dermal and inhalation) for which there is reliable information.

3.5 Cumulative assessment

The *Pest Control Products Act* requires that the PMRA consider the cumulative non-occupational exposure to pesticides with a common mechanism of toxicity, based on the likelihood that people may be exposed to more than one of these pesticides at the same time. Accordingly, assessments of potential common mechanisms of toxicity with other pesticides were undertaken for copper.

For the current evaluation, the PMRA did not identify information indicating that copper shares a common mechanism of toxicity with other registered pest control products. Therefore, there is no requirement for a cumulative health risk assessment at this time.

3.6 Maximum residue limits

The specification of a maximum residue limit for copper was not required for the proposed non-food use of the end-use product.

3.7 Health incident reports

As of 23 August 2024, no human or domestic animal incidents involving copper, present as cuprous oxide and three human incident reports (1 minor, 2 moderate) involving copper, present as cupric oxide have been submitted to the PMRA. In all three incidents, exposure occurred through contact with wood that had been treated with cupric oxide and were therefore not deemed relevant to the use pattern of the products.

4.0 Impact on the environment

The major new uses for copper (present as cupric oxide) and its associated end-use product, Corning Guardiant Antimicrobial Particles (containing copper present as cuprous oxide) are only for indoor use. An environmental assessment was not required because environmental exposure from these indoor uses will be negligible.

For a review of the environmental fate and toxicology of copper, refer to:

- Proposed Re-evaluation Decision, PRVD2009-04, *Copper Pesticides*; and,
- Re-evaluation Decision, RVD2010-05, *Copper Pesticides.*

5.0 Value

The copper particles in Corning Guardiant Antimicrobial Particles offer a novel method of in-can and dry-film preservation in water-based paints.

In addition, bacteria and viruses are able to survive on multiple surfaces. As a result, the surfaces can become involved in disease transmission through fomite transfer, especially in high traffic areas. While sanitizing or disinfecting of surfaces can reduce transmission, certain areas such as

interior walls are often overlooked in terms of cleaning. While interior walls can be wiped down with disinfectant, it is both time-consuming and potentially damaging to the surface. Corning Guardiant Antimicrobial Particles can be used in formulating paint and coatings registered under the *Pest Control Products Act* that have residual efficacy against viruses and bacteria on painted surfaces to supplement existing infection control and cleaning practices.

All formulators wanting to use Corning Guardiant Antimicrobial Particles for residual indoor hard surface efficacy are responsible for registering their pesticide products under the *Pest Control Products Act*.

Corning Guardiant Antimicrobial Particles

The registrant submitted data from multiple laboratory studies to support claims of protecting paint formulations from deterioration caused by yeast and bacteria. The in-can and dry film preservation studies followed protocol ASTM D2574, mixing the copper glass particles with 100 mL of biocide-free paint and inoculating it with individual microorganisms.

These studies demonstrated that acceptable inhibition of yeast and bacteria was achieved with rates as low as 1 g per 3.78 L of paint.

In order to support the claims that the paints and coatings formulated with the product may also offer residual efficacy, different paints (both with and without varying concentrations of Cu-Glass) were assessed for efficacy against representative bacteria and viruses. The minimum efficacy threshold of a three-log reduction (99.9%) was reached with the proposed rate range, in the presence of a 5% fetal bovine serum soil load, on all painted surfaces for all tested microorganisms within two hours of exposure.

6.0 Pest control product 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, i.e., those that meet all four criteria outlined in the policy: persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*. The *Pest Control Products Act* requires that the TSMP be given effect in evaluating the risks of a product.

During the review process, copper (present as cupric oxide in the technical grade active ingredient and cuprous oxide in the end-use product) and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the conclusion that Cupric Oxide and its transformation products do not meet all of the TSMP Track 1 criteria.

Please refer to the Proposed Re-evaluation Decision, PRVD2009-04, *Copper Pesticides* for further information on the TSMP assessment.

6.1 Formulants and contaminants of health or environmental concern

During the review process, contaminants in the active ingredient as well as formulants and contaminants in the end-use products are compared against Parts 1 and 3 of the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.[6] The list is used as described in the PMRA Science Policy Note SPN2020-01[7] and is based on existing policies and regulations, including the *Toxic Substance Management Policy* and *Formulants Policy*,[8] and taking into consideration the *Ozone-depleting Substances and Halocarbon Alternatives Regulations* under the *Canadian Environmental Protection Act, 1999, (*substances designated under the *Montreal Protocol).*

The PMRA has reached the conclusion that Cupric Oxide and the end-use product, Corning Guardiant Antimicrobial Particles, contain lead at maximum levels of 22.1 ppm and 8.04 ppm, respectively. These levels have been assessed by the PMRA to be acceptable. The products do not contain any other formulants or contaminants identified in the *List of Pest Control Product Formulants and 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.

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

6 SI/2005-114, last amended on June 24, 2020. See Justice Laws website, Consolidated Regulations, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern.*

7 PMRA's Science Policy Note SPN2020-01, Policy on the List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under paragraph 43(5)(b) of the Pest Control Products Act

8 DIR2006-02, Formulants Policy and Implementation Guidance Document

7.0 Proposed regulatory decision

Health Canada's PMRA, pursuant to subsection 28(1) of the *Pest Control Products Act*, is proposing registration for the sale and use of Cupric Oxide, containing the active ingredient copper (present as cupric oxide) and Corning Guardiant Antimicrobial Particles containing the active ingredient copper (present as cuprous oxide), as an in-can and dry-film preservative against bacteria and yeast.

Corning Guardiant Antimicrobial Particles may also be used to formulate paints and coatings registered under the *Pest Control Products Act* that have residual antimicrobial effectiveness after application to indoor hard surfaces (kills 99.9% of bacteria and viruses within two hours on painted surfaces). All formulators wanting to use Corning Guardiant Antimicrobial Particles for residual indoor hard surface efficacy are responsible for registering their pesticide products under the *Pest Control Products Act*.

An evaluation of available scientific information found that, under the approved conditions of use, the health and environmental risks and the value of the pest control products are acceptable.

List of abbreviations

♀	female
µg	microgram
°C	degrees centigrade
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetres
DIR	Directive
DNA	deoxyribonucleic acid
EP	end-use product
FBS	fetal bovine serum
g	gram
HDPE	high density polyethylene
hdt	highest dose tested
hr	hour
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{ow}	n–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LDPE	low density polyethylene
MAS	maximum average score
MIS	maximum irritation score
mg	milligram
MMAD	mass median aerodynamic diameter
MRL	maximum residue limit
PCPA	Pest Control Product Act
pK_a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRVD	proposed re-evaluation decision
RH	relative humidity
RNA	ribonucleic acid
RVD	re-evaluation decision
SPN	Science Policy Note
TGAI	technical grade active ingredient
TSMP	Toxic Substances Management Policy
w/w	weight for weight

Appendix I Tables and figures

Table 1 Toxicity profile of Corning Guardiant Antimicrobial Particles (27% w/w cuprous oxide)

(Effects are known or assumed to occur in both sexes unless otherwise noted.)

Study type/Animal/PMRA #	Study results
Acute toxicity studies	
Acute oral toxicity (Up and Down study) Rat, Sprague-Dawley (♀) PMRA 3241854	LD_{50} of 1750- 5000 mg/kg bw 5000 mg/kg bw (hdt): adverse clinical reactions (↓ activity, distended abdomen, ↓ defecation, blue feces/urine, hunched posture, hypothermia, emaciation, ocular discharge and piloerection) resulting in death, abnormal necropsy results (crusted nasal area, stained anogenital area, discoloured lungs, liver, spleen and contents in the gastrointestinal tract, and gas in the gastrointestinal tract). **Slight acute toxicity**
Acute dermal toxicity Rat, Sprague-Dawley PMRA 3241855	LD_{50} > 5050 mg/kg bw (combined) Low toxicity
Acute inhalation toxicity (Nose-only exposure) Rat, Sprague-Dawley PMRA 3241856	LC_{50} (combined) > 2.29 mg/L MMAD = 3.3 µm Mild signs of piloerection and ↓ activity resolved by Day 1. Discoloured lungs. Low toxicity
Eye irritation Rabbit, New Zealand White PMRA 3241857	MAS = 4/110 (24, 48 and 72 hrs) MIS =14.67 at 1 hr Conjunctivitis, resolved by Day 4. Mildly irritating
Skin Irritation Rabbit, New Zealand White PMRA 3241858	MAS = 0/8 (at 24, 48 and 72 hrs) MIS = 0 Evidence of test substance staining, resolved by Day 2. Non-irritating

Study type/Animal/PMRA #	Study results
Dermal sensitization (modified Buehler) Guinea pigs – Hartley Albino PMRA 3241859	Negative Not a dermal sensitizer

References

A. List of studies/Information submitted by registrant

1.0 Chemistry

PMRA document number	Reference
3376435	2022, American Chemet GLP Study for Cupric Oxide [CBI removed], DACO: 2.13.4 CBI
3241847	2021, Description of Materials Used to Produce the Product, DACO: 3.2.1 CBI
3241848	2021, Description of Production Process, DACO: 3.2.2 CBI
3241849	2021, Discussion of Formation of Impurities, DACO: 3.2.3 CBI
3241851	2015, Physical/Chemical Product Properties of Corning Antimicrobial Particles, DACO: 3.5, 3.5.1, 3.5.11, 3.5.12, 3.5.13, 3.5.15, 3.5.2, 3.5.3, 3.5.6, 3.5.7, 3.5.8, 3.5.9 CBI
3241852	2018, Corning Guardiant Antimicrobial Particles Accelerated Storage Stability with Corrosion Characteristics, DACO: 3.5.10, 3.5.14 CBI
3274035	2021, DACO 3.5.4 - Formulation Type, DACO: 3.5.4 CBI
3274036	2021, DACO 3.5.5 - Container Material and Description, DACO: 3.5.5
3544463	2024, Description of Formulation Process Clarifications, DACO: 3.2.2 CBI

2.0 Human and animal health

PMRA document number	Reference
3241854	2017, Copper Glass Particles Acute Oral Toxicity (UDP) in Rats, DACO: 4.6.1
3241855	2017, Copper Glass Particles Acute Dermal Toxicity in Rats, DACO: 4.6.2
3241856	2018, Guardiant Antimicrobial Particles Acute Inhalation Toxicity in Rats, DACO: 4.6.3
3241857	2017, Copper Glass Particles Acute Eye Irritation in Rabbits, DACO: 4.6.4
3241858	2017, Copper Glass Particles Acute Dermal Irritation in Rabbits, DACO: 4.6.5
3241859	2017, Copper Glass Particles Skin Sensitization in Guinea Pigs, DACO: 4.6.6
3241879	2015, 2015, Health Effects Waiver Requests for Copper (II) Oxide in Corning Antimicrobial Particles, DACO: 12.7.4
3241860	2021, Guardiant Use Description Scenario, DACO: 5.2
3547780	2024, Part 4 Toxicology Studies Test Substance Clarification, DACO: 4.6
3616519	2024, Clarification Response on Use Pattern for Corning Guardiant Antimicrobial Particles

3.0 Environment

None

4.0 Value

PMRA document number	Reference
3241831	2015, In can preservation Testing (ASTM D2574) of Cu-Glass particles, DACO: 10.2.3.2(E)
3241832	2020, Test for Continuous Viral reduction on Coated Surfaces; EPA-approved protocol granted to Corning Incorporated - Commercial Paint 2, DACO: 10.2.3.2(E)
3241833	2020, Test for Continuous Viral reduction on Coated Surfaces; EPA-approved protocol granted to Corning Incorporated - Commercial Paint 1, DACO: 10.2.3.2(E)
3241834	2018, Antiviral Activity and Sanitizing Efficacy of Corning's Test Surfaces, DACO: 10.2.3.2(E)
3241835	2018, Antiviral Activity and Sanitizing Efficacy of Corning's Test Surfaces, DACO: 10.2.3.2(E)
3241836	2019, Evaluation of Bacterial activity of antimicrobial paint coated surfaces, DACO: 10.2.3.2(E)
3241837	2019, Evaluation of Bacterial activity of antimicrobial paint coated surfaces, DACO: 10.2.3.2(E)
3241838	2019, Antiviral Activity and Sanitizing Efficacy of Corning's Test Surfaces, DACO: 10.2.3.2(E)
3241839	2019, Evaluation of bacterial activity of antimicrobial paint coated surfaces, DACO: 10.2.3.2(E)
3241840	2019, Evaluation of bacterial activity of antimicrobial paint coated surfaces, DACO: 10.2.3.2(E)
3241841	2019, Antiviral Activity and Sanitizing Efficacy of Corning's Test Surfaces, DACO: 10.2.3.2(E)
3241842	2019, Antiviral Activity and Sanitizing Efficacy of Corning's Test Surfaces, DACO: 10.2.3.2(E)
3250583	2021, In-Can Challenge Test of Four Paint Samples based on ASTM D2574 Test Method [with additional 3rd challenge], DACO: 10.2.3.2(E)