Proposed Registration Decision PRD2016-12

# Copper (present as cuprous oxide)

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# Overview

## Proposed Registration Decision for Copper (Present as Cuprous Oxide)

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of SCM Metal Products Cuprous Oxide and Cupron Enhanced EOS, containing the technical grade active ingredient copper (present as cuprous oxide). Cupron Enhanced EOS is an end-use product made of a plastic matrix that contains cuprous oxide as the active ingredient, which can be shaped and formed into solid surfaces used in the manufacture and fabrication of non-food contact touch surfaces and objects to be used in various areas.

Please note that a Proposed Re-evaluation Decision on copper has been published under PRVD2009-04, *Copper Pesticides*.

An evaluation of available scientific information found that, under the approved conditions of use, the products have value and do not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of SCM Metal Products Cuprous Oxide and Cupron Enhanced EOS.

## What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment. These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the

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

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

assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

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

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

## What Is Copper (Present as Cuprous Oxide)?

Cuprous oxide is not currently registered for use as a sanitizer in Canada. However, it is registered for use as a wood preservative, material preservative and for use in antifouling paints. Copper toxicity to microorganisms is achieved through several parallel mechanisms, primarily by disrupting membrane integrity which inevitably leads to loss of cell viability.

## Health Considerations

### Can Approved Uses of Copper (Present as Cuprous Oxide) Affect Human Health?

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

Potential exposure to the technical grade active ingredient copper, present as cuprous oxide, may occur when handling, installing, and touching products fabricated with the end-use product, which is a polymer matrix embedded with the active ingredient.

When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Copper, present as cuprous oxide, is of low acute toxicity, severely irritating to the eyes and skin, and is not a dermal sensitizer.

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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*.

Due to the physical nature of the end-use product with the active ingredient being impregnated in a polymer matrix, dermal exposure to copper is expected to be low under normal conditions of use. The end-use product is not likely to be toxic from the dermal route, or sensitizing or irritating. The use of copper oxide in consumer and medical products that come in contact with skin has been reported to be safe.

Based on a long history of use of copper in fabricated products, it is not expected that exposure to copper from the surface materials fabricated with the end-use product will result in short-term toxicity, developmental toxicity, or genotoxicity.

**Residues in Water and Food**

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

The proposed new use of copper, present as cuprous oxide, is for non-food contact touch surfaces; therefore, there is no concern for dietary exposure. Dietary risks from food and drinking water are negligible.

**Risks in Residential and Other Non-Occupational Environments**

**Estimated risk for residential and other non-occupational exposure is not of concern.**

Residential exposure or exposure from other non-occupational environments to the products fabricated with the end-use product Cupron Enhanced EOS is possible when residents/consumers/public come in contact with those products (for example, door handles, railings, etc.) during handling, use or clean-up and maintenance activities or other activities of contact in public places. The duration of dermal exposure may be short-term or long-term depending on the nature of the products, their uses and activities associated with them. There is no risk anticipated from dermal exposure under normal conditions of use because the active ingredient is in a bound form in the fabricated products and is not likely to be transferred on contact with skin in appreciable quantities from such surfaces or be readily absorbed by the skin.

**Occupational Risks From Handling the End-use Product Cupron Enhanced EOS**

**Occupational risks are not of concern when Cupron Enhanced EOS is used according to the proposed label directions, which include protective measures.**

Risks to individuals handling and installing products fabricated with Cupron Enhanced EOS are not of concern because of low dermal exposure, low acute toxicity of copper, and the active ingredient being bound in a plastic and not readily absorbed in quantities to cause harmful effects.

## Environmental Considerations

No environmental assessment was required for these applications as environmental exposure is limited to the types of products that will be manufactured with the end-use product Cupron Enhanced EOS.

## Value Considerations

### What Is the Value of Cupron Enhanced EOS?

**Cupron Enhanced EOS is a plastic matrix that contains cuprous oxide as an active ingredient that can be shaped and formed into solid surfaces used in the manufacture and fabrication of non-food contact touch surfaces in various areas to deliver continuous and ongoing antibacterial action.**

The use of biocidal hard surfaces in various settings (for example, medical settings), such as Cupron Enhanced EOS, in direct or indirect contact with patients, is capable of reducing the bacterial burden between routine disinfection procedures, and will help diminish the potential for cross-contamination. Because the antimicrobial activity comes from the surface itself, the sanitizing activity is continuous and cannot be removed or wiped off from the surface.

## 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.

Due to the physical nature of the end-use product, which is a plastic sheet impregnated with the active ingredient, and the toxicology profile of the end-use product characterized from the available published information on the copper embedded material for biocide use, the proposed end-use product raises no hazards of concern. No exposure mitigation measures are required on the end-use product label.

## Next Steps

Before making a final registration decision on copper (present as cuprous oxide), the PMRA will consider any comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward any comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

## Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on copper (present as cuprous oxide) (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

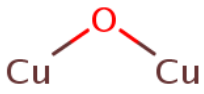
# Science Evaluation

## Copper (present as cuprous oxide)

Please note that a Proposed Re-evaluation Decision on copper has been published under PRVD2009-04, *Copper Pesticides*. The information captured herein relates to new information provided to the PMRA in support of a major new use for cuprous oxide.

## 1.0 The Active Ingredient, Its Properties and Uses

### 1.1 Identity of the Active Ingredient – Copper (present as cuprous oxide)

| | |
|---|---|
| **Active substance** | Cuprous oxide |
| **Function** | Hard surface sanitizer, material preservative |
| **Chemical name** | |
| **1. International Union of Pure and Applied Chemistry (IUPAC)** | Copper(I) oxide<br>or copper(1+) oxide<br>or cuprous oxide |
| **2. Chemical Abstracts Service (CAS)** | Copper oxide ($Cu_2O$) |
| **CAS number** | 1317-39-1 |
| **Molecular formula** | $Cu_2O$ |
| **Molecular weight** | 143.1 |
| **Structural formula** |  |
| **Purity of the active ingredient** | 88.44% as copper |

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

**Technical Product – SCM Metal Products Cuprous Oxide**

Refer to PRVD2009-04.

**End-Use Product – Cupron Enhanced EOS**

| Property | Result |
|---|---|
| Colour | Grey or beige |
| Odour | None |
| Physical state | Solid |
| Formulation type | Solid |
| Guarantee | 14.50% as copper |
| Container material and description | Solid plastic matrix |
| Density | 2.4 g/cm$^3$ |
| pH of 1% dispersion in water | N/A, product is a solid |
| Oxidizing or reducing action | N/A, solid plastic matrix |
| Storage stability | Stable, solid polymer |
| Corrosion characteristics | N/A, solid plastic matrix |
| Explodability | N/A, solid plastic matrix |

## 1.3 Directions for Use

Cupron Enhanced EOS is an end-use product made of a plastic matrix that contains cuprous oxide as the active ingredient, which can be shaped and formed into solid surfaces used in the manufacture and fabrication of non-food contact touch surfaces and objects to be used in various areas:

- Healthcare facilities
- Community facilities (public and commercial buildings)
- Common areas in residential buildings (for example, apartment/condo buildings)
- Mass transit facilities
- Kitchen and bathrooms in homes and apartments

Cupron Enhanced EOS may be used in hospitals, other healthcare facilities, and various public commercial and residential buildings. However, this product must not be used for direct food contact or food packaging uses.

## 1.4 Mode of Action

Copper toxicity to microorganisms is achieved through several parallel mechanisms. Literature suggests that these include plasma membrane permeabilization, membrane lipid peroxidation, alteration of proteins and inhibition of their biological assembly and activity, and denaturation of nucleic acids. It is likely that the first site that copper damages is the microorganism's envelope. Extensive copper-induced disruption of membrane integrity inevitably leads to loss of cell viability.

# 2.0 Methods of Analysis

## 2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and impurities in the technical product have been validated and assessed to be acceptable for the determinations.

## 2.2 Method for Formulation Analysis

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

# 3.0 Impact on Human and Animal Health

## 3.1 Toxicology Summary

The technical SCM Metal Products Cuprous Oxide is currently registered and there have been no changes made to the product's chemistry that would trigger the requirement for additional toxicology data. Copper-containing pesticides, including SCM Metal Products Cuprous Oxide, were re-evaluated by the PMRA (PRVD2009-04 and Re-evaluation Decision RVD2010-05, *Copper Pesticides*) and these re-evaluations were used as the primary basis for the current assessment. The toxicology profile of copper, present as cuprous oxide is characterized as being of low acute toxicity by the oral, dermal, and inhalation routes, severely irritating to the eyes and skin, and is not a dermal sensitizer.

To support the registration of the end-use product Cupron Enhanced EOS, data waiver rationales were submitted in lieu of studies for oral toxicity, dermal toxicity, inhalation toxicity, eye irritation, dermal irritation, and dermal sensitization. The waiver rationales argued that the routes of entry associated with toxicity testing were not applicable to this end-use product. The end-use product is a polymeric matrix that contains cuprous oxide that can be shaped and formed into solid surfaces used in the manufacture and fabrication of non-food contact touch surfaces in residential buildings and publicly accessible facilities. As the physical form of the final product is a thin slab, it is not practical for testing on animals to determine its acute toxicity, its dermal and ocular irritation or dermal sensitization potential, and the waiver was accepted.

To be effective as an embedded surface material sanitizer, free copper ions must be present at the surface of the polymer matrix, so dermal contact exposure is likely to occur from normal use. However, the end-use product is not likely to be toxic from dermal route or sensitizing or irritating based on published information on copper-oxide embedded materials.

The use of copper oxide in consumer and medical products that come in contact with skin is reported to be safe. Published studies on the biocidal use of copper impregnated materials in medical devices and consumer products, such as wound dressings, antiviral respiratory masks, antifungal socks, diapers, antiviral gloves and filters, antibacterial self-sterilizing fabrics, and anti-dust mite mattress covers demonstrated no adverse effects.

In nine clinical trials and several non-clinical studies, copper oxide products have been found to be non-irritating, non-sensitizing, and safe to use, with no adverse reactions reported when the exposure is with both intact and broken skin. Also, application of ointment preparations containing copper to skin in concentrations up to 20% w/w did not result in adverse toxic effects in humans.

Animal testing with copper impregnated materials demonstrated no skin sensitizing or irritation properties. In Guinea pigs, maximization test using test fabrics extracts (containing 0.4% copper oxide w/w) showed no allergic skin reactions. In rabbits, skin irritation test with products containing 0.4% to 3% copper oxide w/w for 4 hour exposure time showed no skin irritation. Toxic effects or clinical signs of toxicity were not exhibited by any of the animals exposed to the treatment.

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 is a naturally occurring metal that occurs in many foods and in drinking water. Copper is also an essential trace element, with adverse effects in humans more likely to result from copper deficiency rather than excess. Humans have efficient mechanisms in place to regulate levels of copper in the body, and as such are generally protected from exposure to excess levels of copper; however, some less common genetic conditions in humans may cause abnormal copper metabolism.

Based on a long history of use of copper in fabricated products, it is not expected that human exposure to copper from the proposed surface material will result in short-term toxicity, developmental toxicity, or genotoxicity.

**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. Information on the reporting of incidents can be found on the Health Canada website. Incidents from Canada were searched for pesticide products containing the active ingredient copper oxide.

As of 16 October 2015, no human, domestic animal or environment incident reports involving copper oxide had been submitted to the PMRA.

## 3.2 Occupational and Bystander Exposure and Risk Assessment

### 3.2.1 Dermal Absorption

Dermal absorption is expected to be negligible because copper, present as cuprous oxide, is bound to a solid polymer matrix, and it is not likely that copper ions will migrate in significant quantities on to skin or be readily available for absorption on dermal contact.

### 3.2.2 Use Description

The end-use product, Cupron Enhanced EOS, is a polymeric matrix into which the active ingredient is homogenously incorporated at the time of manufacture, and is intended to act as a biocidal surface with continuous action. Cupron Enhanced EOS is to be sold to companies that will install the material as a surface (non-food contact) or as components to be included onto or in furniture and devices used in settings where individuals are at high risk of exposure to disease causing bacteria. The proposed use sites for the end-use product are in Healthcare Facilities, Community Facilities (including various public and commercial buildings), Residential Buildings (including homes, apartments, and other residences), and Mass Transit Facilities.

### 3.2.3 Mixer, Loader, and Applicator Exposure and Risk

Due to the physical nature of the end-use product, which is a slab polymeric matrix, and its non-conventional use as a material in fabricated products, there is no mixer/loader/applicator occupational exposure. Workers are expected to be exposed dermally when handling and installing products fabricated with Cupron Enhanced EOS, and the magnitude of exposure is expected to vary depending on the nature and duration of a given task. There is negligible risk from such exposures as copper, present as cuprous oxide, has low toxicity and is largely impregnated within the polymer matrix.

### 3.2.4 Post-application Exposure and Risk

Due to its non-conventional use as a material in fabricated products, not in a sprayable or spreadable form to a specific area, there is no post-application exposure or risk associated with the proposed use.

### 3.2.5 Residential and Bystander Exposure and Risk

Residential exposure to the products fabricated with Cupron Enhanced EOS is likely when residents/domestic-users come in contact with installed products during handling, use or clean-up and maintenance activities or other activities involving direct contact. The duration of dermal exposure may be short-term or long-term depending on the nature of the products, their uses and activities associated with them. There is no risk anticipated from dermal exposure because the active ingredient is in a bound form in the fabricated products and it is not likely to be transferred onto skin on contact in appreciable amounts or absorbed readily in a concentration that is detrimental to human health under normal conditions.

Bystander exposure is not likely as the end-use product is not in a sprayable or spreadable form to cause bystander exposure.

### 3.3 Food Residue Exposure Assessment

#### 3.3.1 Food and Drinking Water

The new use is for non-food contact touch surfaces; therefore, there is no concern from food and drinking water exposure.

#### 3.3.2 Maximum Residue Limits (MRLs)

Specification of MRLs is not required because there are no proposed food uses and the end-use product is not intended for food contact surfaces. Food and drinking water exposure is therefore not anticipated.

## 4.0 Impact on the Environment

No environmental assessment was required for these applications.

## 5.0 Value

### 5.1 Consideration of Benefits

The antibacterial activity coming from the copper that is embedded in the solid surfaces is an important part of the value of this product when compared to sanitizers applied by spray, which have to be re-applied often, especially if the treated surfaces are touched or contaminated frequently during a day. This is particularly useful on surfaces that are touched by a high number of people in the interval between the standard cleaning procedures, such as in public transportation vehicles (for example, grab bars and handles), or in public and health care facilities (for example, door push plates).

An incidence rate of 200,000 patients per year has been reported to have acquired infections while receiving healthcare in Canada. The Public Health Agency of Canada indicated that there is a range of infection pathways including touching contaminated surfaces. Infections greatly increase the morbidity and mortality of the patient and increase patient suffering, as well as economically impact the cost of healthcare. These surfaces will provide a supplemental antimicrobial action between routine cleanings, which could be an additional tool in decreasing the amount of bacteria present in public environments.

In spite of the long history of use of copper, no microorganisms that are highly resistant to copper have been found, but only microorganisms with reduced copper sensitivity (increased copper tolerance). The increased tolerance to copper was found to be associated with the amount of soluble copper and not with the total amount of copper. Since cuprous oxide is a non-soluble form of copper, there are no resistance management issues expected from its use.

### 5.2 Effectiveness Against Pests

Twelve laboratory trials have demonstrated that Cupron Enhanced EOS surfaces are effective at achieving 99.9% reduction for several Gram-negative and Gram-positive bacteria following a 2-hour contact period. The self-sanitizing tests have shown that the efficacy of the copper does not diminish following physical contact and abrasion, and the continuous sanitizing tests have shown the efficacy of copper at reducing bacterial populations by 90% or more after multiple inoculations with high bacteria concentration.

### 5.3 Non-Safety Adverse Effects

No non-safety adverse effects have been reported from the use of Cupron Enhanced EOS in the manufacture and fabrication of non-food contact touch surfaces.

### 5.4 Supported Uses

See Table 2, Appendix 1.

## 6.0 Pest Control Product Policy Considerations

### 6.2 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: that is, 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*].

As indicated in PRVD2009-04 and based on an assessment of Copper, present as cuprous oxide, in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Copper, present as cuprous oxide, do not meet the Track 1 criteria, and is not considered a Track 1 substance.

- There are also no formulants, contaminants or impurities present in the end-use product that would meet the TSMP track 1 criteria.

### 6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the

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

end-use products are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette.*[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including DIR99-03 and DIR2006-02[8], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade Copper, present as cuprous oxide (SCM Metal Products Cuprous Oxide) and the end-use product Cupron Enhanced EOS do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette.*

- No other impurities of toxicological concern as identified in Regulatory Directive DIR98-041[5], Section 2.13.4, or TSMP Track 1 substances as identified in Regulatory Directive DIR99-03, Appendix II, are expected to be present in the technical product of Copper (present as cuprous oxide).

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

# 7.0 Summary

## 7.1 Human Health and Safety

The toxicology profile of the registered technical grade active ingredient is characterized as before. It is severely irritating to the eyes and skin. The data waiver requests for the end-use product were found to have merit and were accepted because toxicology testing of the end-use product is not relevant to the anticipated exposure.

The end-use product is not likely to be toxic from dermal route or sensitizing or irritating based on published studies on copper-oxide embedded materials, where no adverse effects were reported.

Based on a long history of use of copper in fabricated products, it is not expected that exposure to copper from the surface materials fabricated with the end-use product will result in short-term toxicity, developmental toxicity, or genotoxicity.

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6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette,* Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613*. Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*.

8 DIR2006-02, PMRA Formulants Policy .

Occupational workers are exposed dermally when handling and installing the products fabricated with Cupron Enhanced EOS. There is negligible risk from such exposure as the active ingredient is bound in a matrix.

There is no risk anticipated from the proposed residential use of the end-use product. Food and drinking water exposure are not expected.

### 7.2 Value

Cupron Enhanced EOS is a plastic matrix that contains cuprous oxide as an active ingredient that can be shaped and formed into solid surfaces used in the manufacture and fabrication of non-food contact touch surfaces in various areas to deliver continuous and ongoing antibacterial action. The use of biocidal hard surfaces in medical settings, in direct or indirect contact with patients, is capable of reducing the bacterial burden between routine disinfection procedures, and will help diminish the potential for cross-contamination. Because the antimicrobial activity comes from the surface itself, the sanitizing activity is continuous and cannot be removed or wiped off from the surface, while spray sanitizers have to be re-applied often, especially if the treated surfaces are touched or contaminated frequently during a day.

## 8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of SCM Metal Products Cuprous Oxide and Cupron Enhanced EOS, containing the technical grade active ingredient copper (present as cuprous oxide), to be used to manufacture products with inherent antimicrobial properties.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

## List of Abbreviations

| | |
|---|---|
| µg | micrograms |
| 1/n | exponent for the Freundlich isotherm |
| a.i. | active ingredient |
| ADI | acceptable daily intake |
| ALS | acetolactate synthase |
| ARfD | acute reference dose |
| atm | atmosphere |
| bw | body weight |
| CAS | Chemical Abstracts Service |
| cm | centimetres |
| Cu | Copper |
| DF | dry flowable |
| DNA | deoxyribonucleic acid |
| $DT_{50}$ | dissipation time 50% (the dose required to observe a 50% decline in concentration) |
| $DT_{75}$ | dissipation time 75% (the dose required to observe a 75% decline in concentration) |
| $EC_{10}$ | effective concentration on 10% of the population |
| $EC_{25}$ | effective concentration on 25% of the population |
| $ER_{25}$ | effective rate for 25% of the population |
| g | gram |
| ha | hectare(s) |
| HDT | highest dose tested |
| Hg | mercury |
| HPLC | high performance liquid chromatography |
| IUPAC | International Union of Pure and Applied Chemistry |
| kg | kilogram |
| $K_d$ | soil-water partition coefficient |
| $K_F$ | Freundlich adsorption coefficient |
| km | kilometre |
| $K_{oc}$ | organic-carbon partition coefficient |
| $K_{ow}$ | *n*–octanol-water partition coefficient |
| L | litre |
| $LC_{50}$ | lethal concentration 50% |
| $LD_{50}$ | lethal dose 50% |
| LOAEL | lowest observed adverse effect level |
| LOEC | low observed effect concentration |
| LOQ | limit of quantitation |
| $LR_{50}$ | lethal rate 50% |
| mg | milligram |
| mL | millilitre |
| MAS | maximum average score |
| MOE | margin of exposure |
| MRL | maximum residue limit |
| MS | mass spectrometry |
| N/A | not applicable |

| | |
|---|---|
| NOAEL | no observed adverse effect level |
| NOEC | no observed effect concentration |
| NOEL | no observed effect level |
| NOER | no observed effect rate |
| N/R | not required |
| NZW | New Zealand white |
| OC | organic carbon content |
| OM | organic matter content |
| PBI | plantback interval |
| PHI | preharvest interval |
| p*K*a | dissociation constant |
| PMRA | Pest Management Regulatory Agency |
| ppm | parts per million |
| RSD | relative standard deviation |
| SC | soluble concentrate |
| $t_{1/2}$ | half-life |
| T3 | tri-iodothyronine |
| T4 | thyroxine |
| TRR | total radioactive residue |
| TSMP | Toxic Substances Management Policy |
| UAN | urea ammonium nitrate |
| UF | uncertainty factor |
| USEPA | United States Environmental Protection Agency |
| UV | ultraviolet |
| v/v | volume per volume dilution |
| w/w | weight/weight |

# Appendix I Tables and Figures

## Table 1 Registered Alternatives (as of December 2015)

| Active Ingredient | Product Name | Registration Number |
|---|---|---|
| Copper metallic | Antimicrobial Copper Alloys Group I | 31172 |
| Copper metallic | Antimicrobial Copper Alloys Group II | 31173 |
| Copper metallic | Antimicrobial Copper Alloys Group III | 31174 |
| Copper metallic | Antimicrobial Copper Alloys Group IV | 31175 |
| Copper metallic | Antimicrobial Copper Alloys Group V | 31176 |
| Copper metallic | Antimicrobial Copper Alloys Group VI | 31177 |

## Table 2 Use (label) Claims Supported

| Proposed label claims | Supported label claims |
|---|---|
| Manufacture and fabrication of touch surface components for use in:<br>o Healthcare facilities<br>o Community facilities (public and commercial buildings)<br>o Common areas in residential buildings (for example, apartment/condo buildings)<br>o Mass transit facilities<br>o Kitchen and bathrooms in homes and apartments | Accepted as proposed |

| Proposed label claims | Supported label claims |
|---|---|
| Laboratory testing has shown that when cleaned regularly this surface: | Laboratory testing has shown that when cleaned regularly this surface: |
| ▪ Reduces bacterial contamination, achieving 99.9% reduction within 2 hours of exposure. | ▪ Accepted as proposed |
| ▪ Kills greater than 99.9% of Gram-negative and Gram-positive bacteria within 2 hours of exposure. | ▪ Accepted as proposed |
| ▪ Delivers continuous and ongoing antibacterial action | ▪ Accepted as proposed |
| ▪ Remains effective in killing greater than 99.9% of bacteria within 2 hours. | ▪ Accepted as proposed |
| ▪ Kills greater than 99.9% of bacteria within two hours and continues to kill 99% of bacteria even after repeated contaminations. | ▪ Accepted as proposed |
| ▪ Helps inhibit the buildup and growth of bacteria within 2 hours of exposure between routine cleaning and sanitizing steps. | ▪ Accepted as proposed |
| ▪ [This product/component name] is made (out of)(from) Cupron Enhanced EOS that continuously kills 99.9% of bacteria left behind [by dirty hands] [on the surface]. | ▪ Accepted as proposed |

# References

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

### 1.0 Chemistry

| PMRA Document Number | Reference |
|---|---|
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| 2442206 | 2014, Chemistry-3.1.1-4,3.2.1,3.5.4-5, 8-EOS, DACO: 3.1.1,3.1.2,3.1.3,3.1.4,3.5.4,3.5.5,3.5.8 |
| 2442208 | 2006, Cupron Copper Enhanced EOS Surface, Product Chemistry, Group A: Product Identity, Composition and Analytical Test Guidelines and Group B: Physical and Chemical Properties Test Guidelines, DACO: 3.2.1,3.2.2,3.3.1,3.4.1,3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2,3.5.3, 3.5.6,3.5.7,3.5.9 CBI |
| 2506898 | 2015, Chemistry-3.4.1-validation-2014-2656, DACO: 3.4.1 CBI |
| 2508409 | 2015, Chemistry-3.2.2-EOS-12jan2015, DACO: 3.2.2 CBI |
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| 2540568 | 2015, Chemistry-3.5-EOS-05june2015-final, DACO: 3.5.1,3.5.10,3.5.11,3.5.12,3.5.13,3.5.14,3.5.15,3.5.2,3.5.3,3.5.4,3.5.5,3.5.6,3.5.7, 3.5.8,3.5.9 |
| 2540569 | Anonymous, 2015, ASTM D792 - Test method a for testing density of solid plastics in water, DACO: 3.5.6 |

### 2.0 Human and Animal Health

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|---|---|
| 2442183 | Gadi Borkow and Jeffrey Gabbay, 2005, Copper as a Biocidal Tool, DACO: 10.2.3.4(A) |
| 2442185 | Gadi Borkow and Jeffrey Gabbay, 2009, Copper, An Ancient Remedy Returning to Fight Microbial, Fungal and Viral Infections, DACO: 10.2.3.4(A) |
| 2442186 | Gadi Borkow, 2012, Using Copper to Fight Microorganisms, DACO: 10.2.3.4(A) |
| 2442187 | Alastair B Monk, Vikram Kanmukhla, Ken Trinder and Gadi Borkow, 2012, Potent bactericidal efficacy of copper oxide impregnated non-porous solid surfaces, DACO: 10.2.3.4(A) |
| 2487134 | 2012, Tox 4.6.1-acute oral-EOS waiver, DACO: 4.6.1 |
| 2487135 | 2012, Tox 4.6.2-acute dermal-EOS waiver, DACO: 4.6.2 |
| 2487136 | 2012, Tox 4.6.3-acute inhalation-EOS waiver, DACO: 4.6.3 |
| 2487137 | Reference: 2012, Tox 4.6.4-acute eye irritation-EOS waiver, DACO: 4.6.4 |
| 2487138 | 2012, Tox 4.6.5-acute dermal irritation-EOS waiver, DACO: 4.6.5 |
| 2487139 | 2012, Tox 4.6.6-sensitization-EOS waiver, DACO: 4.6.6 |

2442211 2014, Overview with references-5.2, 10.2.-2,4,10.3.2,10.4, 10.5.3, DACO: 10.2.1,10.2.2,10.2.4,10.3.2,10.4,10.5.3,5.2
2442204 Gadi Borkow, 2012, Safety of Using Copper Oxide in Medical Devices and Consumer Products, DACO: 10.3.2
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2442188 Gadi Borkow, Alastair Monk, 2012, Fighting nosocomial infections with biocidal non-intrusive hard and soft surfaces, DACO: 10.2.3.4(A)
2442189 2012, Efficacy Evaluation of a Copper Enhanced Hard Surface as a Sanitizer, DACO: 10.2.3.4(A)
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2442192 2012, Efficacy Evaluation of a Continuous Bacterial Contamination Reduction on a Copper Enhanced Hard Surface, DACO: 10.2.3.4(A)
2442193 2012, Efficacy Evaluation of a Continuous Bacterial Contamination Reduction on a Copper Enhanced Hard Surface Supplemental, DACO: 10.2.3.4(A)
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2442203 Gadi Borkow, Steve S. Zhou, Tom Page, Jeffrey Gabbay, 2010, A Novel Anti-Influenza Copper Oxide Containing Respiratory Face Mask, DACO: 10.2.3.4(A)

2442204 Gadi Borkow, 2012, Safety of Using Copper Oxide in Medical Devices and Consumer Products, DACO: 10.3.2

## B. Additional Information Considered

### i) Published Information

#### 1.0 Human and Animal Health

http://ceqg-rcqe.ccme.ca/download/en/272. (Canadian Soil Quality Guidelines for the Protection of Environmental and Human Health, Nickel)

http://ceqg-rcqe.ccme.ca/download/en/262. (Canadian Soil Quality Guidelines for the Protection of Environmental and Human Health, Chromium)

http://www.hc-sc.gc.ca/dhp-mps/prodnatur/legislation/docs/eq-paq-eng.php. (Quality of Natural Health Products Guide, 2015)

http://www.hc-sc.gc.ca/fn-an/consult/2014-daily-value-valeurs-quotidiennes/document-consultation-eng.php. (Health Canada's proposed Changes to the Daily Values (DVs), 2014)

http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=92F47C5D-1. (FederaL Environmental Quality Guidelines, Cobalt)

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003586.pdf. (European Medicines Agency, Guideline on the Specification Limits for Residues of Metal Catalysts or Metal Reagents)

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http://www.fasebj.org/content/18/14/1728.full (Putting copper into action: copper-impregnated products with potential biocidal activities).

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## 2.0 Value

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