Cuprous Oxide (CAS# 1317-39-1) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared for:

Washington State Department of Ecology

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October 17, 2014

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GreenScreen® Executive Summary for Cuprous Oxide (CAS #1317-39-1)

Cuprous oxide is a chemical that functions as the active ingredient in antifouling paints for marine use. Additionally, it is used as a fungicide and a catalyst (HSDB 2003).

Cuprous oxide was assigned a GreenScreen® Benchmark Score of 1 ("Avoid – Chemical of High Concern") as it has Very High ecotoxicity (chronic aquatic toxicity (CA)) and Very High persistence (P). This corresponds to GreenScreen® benchmark classification 1c in CPA 2011. Because this chemical received an LT-P1 (List Translator – Potential Benchmark 1) score, a targeted GreenScreen® assessment is required by the scope of work. However, as this chemical is the chemical to be replaced, a full GreenScreen® was performed in order to provide the most data available on the chemical to be substituted. Data gaps exist for endocrine activity (E), single and repeated dose neurotoxicity (Ns and Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), cuprous oxide meets the requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if cuprous oxide were assigned a High score for the data gaps endocrine activity (E), neurotoxicity (repeated exposure (Nr*)), and respiratory sensitization (SnR*), it would be categorized as a Benchmark 1 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:
As a standard approach for GreenScreen® evaluations, all exposure routes (oral, dermal and inhalation) were evaluated together, so the GreenScreen® Benchmark Score of 1 ("Avoid – Chemical of High Concern") is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for Cuprous Oxide

C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	**L**	**L**	**M**	DG	**M**	DG	**M**	DG	DG	**L**	DG	**L**	*M*	**vH**	**vH**	**vH**	*M*	*L*	*L*

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated values, authoritative B lists, screening lists, weak analogues, and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e., vH, H, M, and L) instead of three (i.e., H, M, and L), and are based on single exposures instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

GreenScreen® Assessment for Cuprous Oxide (CAS #1317-39-1)

Method Version: GreenScreen® Version 1.2[1]
Assessment Type[2]: Certified

Chemical Name: Cuprous Oxide

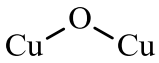
CAS Number: 1317-39-1

GreenScreen® Assessment Prepared By:
Name: Emily Golden, M.F.S.
Title: Toxicologist
Organization: ToxServices LLC
Date: September 21, 2014
Assessor Type: Licensed GreenScreen® Profiler

Quality Control Performed By:
Name: Bingxuan Wang, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: October 17, 2014

Confirm application of the *de minimus* rule[3]: N/A

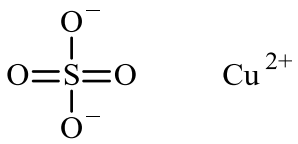
Chemical Structure(s):



Also called: Brown copper oxide; copper hemioxide; copper sandoz; dicopper monoxide; Perecot (ChemIDplus 2014)

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
As limited data were identified for cuprous oxide, several soluble cupric compounds were used as surrogates, as the copper ion is expected to be the species of toxicological concern. These chemicals are also used as read across chemicals for cuprous oxide in the REACH Dossier (ECHA 2014). However, as cuprous oxide has very low solubility in water, data on these soluble cupric compounds were interpreted with caution due to potential difference in bioavailability. The structures of these surrogates are identified below:

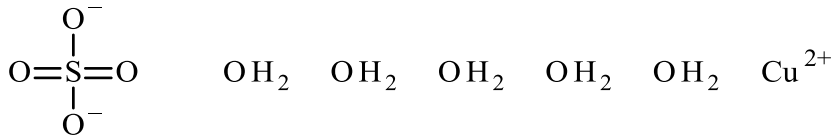
Copper Sulfate



(CAS #7758-98-7)

[1] Use GreenScreen® Assessment Procedure (Guidance) V1.2
[2] GreenScreen® reports are either "UNACCREDITED" (by unaccredited person), "AUTHORIZED" (by Authorized GreenScreen® Practitioner), "CERTIFIED" (by Licensed GreenScreen® Profiler or equivalent) or "CERTIFIED WITH VERIFICATION" (Certified or Authorized assessment that has passed GreenScreen® Verification Program)
[3] Every chemical in a material or formulation should be assessed if it is:
1. intentionally added and/or
2. present at greater than or equal to 100 ppm

Copper (II) Sulfate Pentahydrate



(CAS #7758-99-8)

Copper Hydroxide

(CAS #1344-69-0)

Identify Applications/Functional Uses: (HSDB 2003)
1. Antifouling paints for marine use
2. Fungicide
3. Pigment
4. Catalyst

GreenScreen® Summary Rating for Cuprous Oxide[4]: Cuprous oxide was assigned a GreenScreen® Benchmark Score of 1 ("Avoid – Chemical of High Concern") as it has Very High ecotoxicity (chronic aquatic toxicity (CA)) and Very High persistence (P). This corresponds to GreenScreen® benchmark classification 1c in CPA 2011, 2012a. Because this chemical received an LT-P1 (List Translator – Potential Benchmark 1) score, a targeted GreenScreen® assessment is required by the scope of work. However, as this chemical is the chemical to be replaced, a full GreenScreen® was performed in order to provide the most data available on the chemical to be substituted. Data gaps exist for endocrine activity (E), single and repeated dose neurotoxicity (Ns and Nr*), and respiratory sensitization (SnR*). As outlined in CPA (2013) Section 12.2 (Step 8 – Conduct a Data Gap Analysis to assign a final Benchmark score), cuprous oxide meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if cuprous oxide were assigned a High score for the data gaps endocrine activity (E), neurotoxicity (repeated exposure(Nr*)), and respiratory sensitization (SnR*), it would be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Cuprous Oxide

C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	**L**	**L**	**M**	DG	**M**	DG	**M**	DG	DG	**L**	DG	**L**	*M*	**vH**	**vH**	**vH**	*M*	*L*	*L*

Note: Hazard levels (Very High (vH), High (H), Moderate (M), Low (L), Very Low (vL)) in *italics* reflect estimated (modeled) values, authoritative B lists, screening lists, weak analogues and lower confidence. Hazard levels in **BOLD** font are used with good quality data, authoritative A lists, or strong analogues. Group II Human Health endpoints differ from Group II* Human Health endpoints in that they have four hazard scores (i.e. vH, H, M, and L) instead of three (i.e. H, M, and L), and are based on single exposures

[4] For inorganic chemicals with low human and ecotoxicity across all hazard endpoints and low bioaccumulation potential, persistence alone will not be deemed problematic. Inorganic chemicals that are only persistent will be evaluated under the criteria for Benchmark 4.

instead of repeated exposures. Please see Appendix A for a glossary of hazard acronyms.

Transformation Products and Ratings:

Identify feasible and relevant fate and transformation products (i.e., dissociation products, transformation products, valence states) **and/or moieties of concern**[5]

Cuprous oxide is considered to be insoluble in water; however, it will dissociate very slowly over time. As a result, cuprous oxide is expected to dissociate to produce the copper ion. The resulting copper ion will be present in the 2+ valence state, as seawater will rapidly oxidize copper from the 1+ valence state to the 2+ valence state as it is released from cuprous oxide (Almeida et al. 2007). As cuprous oxide has a Benchmark of 1, the List Translator scores of transformation products will not further affect the Benchmark of the parent compound.

Functional Use	Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	Feasible and Relevant?	List Translator Results[6,7]
Copper Boat Paint	Throughout	Dissociation/oxication	Copper Ion (Cu^{2+})	15158-11-9	Y	LT-P1

Introduction

Cuprous oxide is an inorganic compound that occurs in nature as cuprite ore. It is a reddish crystalline powder that is formed at high temperatures through oxidation (Brady et al. 2002). Cuprous oxide has several functional uses, such as the active ingredient in anti-fouling boat paints. Additionally, it is used in pigments, as a fungicide, and a catalyst in analytical chemistry (HSDB 2003).

ToxServices assessed cuprous oxide against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.69 (GreenScreen® Hazard Assessment) (ToxServices 2013).

GreenScreen® List Translator Screening Results

The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to identify GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2014) is an online list-searching tool that is used to screen chemicals against the List Translator electronically. It checks all of the lists in the List Translator with the exception of the U.S. Department of Transportation (U.S. DOT) lists (U.S. DOT 2008a,b) and these should be checked separately in conjunction with running the Pharos query. The output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for cuprous oxide can be found in Appendix C and a summary of the results can be found below:

- EC-CLP/GHS Hazard Statements (EU H-Statements)
  - H400 – Aquatic Acute 1 – Very toxic to aquatic life – GreenScreen Benchmark Unspecified (LT-U) – occupational hazard only

[5] A moiety is a discrete chemical entity that is a constituent part or component of a substance. A moiety of concern is often the parent substance itself for organic compounds. For inorganic compounds, the moiety of concern is typically a dissociated component of the substance or a transformation product.
[6] The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen® benchmark 1 chemicals (CPA 2012b). Pharos (Pharos 2014) is an online list-searching tool that is used to screen chemicals against the lists in the List Translator electronically.
[7] The way you conduct assessments for transformation products depends on the Benchmark Score of the parent chemical (See Guidance).

- EC-Risk Phrases (EU R-Phrases)
    - R50/53: Very toxic to aquatic organisms, may cause long term adverse effects in the aquatic environment – GreenScreen Benchmark Unspecified (LT-U) – occupational hazard only
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 9.1A (algal) – Very ecotoxic in the aquatic environment – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 9.1A (crustacean) – Very ecotoxic in aquatic environment – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 9.1A (fish) – Very ecotoxic in aquatic environment – GreenScreen Benchmark Unspecified (LT-U)
- EC-CLP/GHS Hazard Statements (EU H-Statements)
    - H410 – Aquatic Chronic 1 – Very toxic to aquatic life with long lasting effects– GreenScreen Benchmark Possible 1 (LT-P1) – occupational hazard only
- EC-Risk Phrases (EU R-Phrases)
    - R22: Harmful if swallowed – GreenScreen Benchmark Unspecified (LT-U)
- EC-CLP/GHS Hazard Statements (EU H-Statements)
    - H302 Harmful if swallowed – GreenScreen Benchmark Unspecified (LT-U)
- Quebec CSST – WHMIS Classifications (WHMIS)
    - Class D1B – Toxic material causing immediate and serious toxic effects – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 6.1D (inhalation) – Acutely toxic – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 6.1D (oral) – Acutely toxic – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 6.4A Irritating to the eye – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 6.9B (inhalation) – Harmful to human target organs or systems – GreenScreen Benchmark Unspecified (LT-U)
- New Zealand HSNO/GHS (GHS-New Zealand)
    - 6.9B (oral) – Harmful to human target organs or systems – GreenScreen Benchmark Unspecified (LT-U)
- Environment Canada – Domestic Substances List (DSL)
    - DSL substances that are persistent – GreenScreen Benchmark Unspecified (LT-U)
- German FEA – Substances Hazardous to Waters (VwVwS)
    - Class 1 Low Hazard to Waters – GreenScreen Benchmark Unspecified (LT-U) – occupational hazard only
- Environment Canada – Domestic Substances List (DSL)
    - Inherently Toxic in the Environment – GreenScreen Benchmark Unspecified (LT-U)
- Environment Canada – Domestic Substances List
    - Inherently Toxic to Humans – DSL substances that meet human health categorization criteria – GreenScreen Benchmark Unspecified (LT-U)

PhysicoChemical Properties of Cuprous Oxide

Cuprous oxide is an inorganic compound with a molecular weight of 143.091 g/mol. It is solid at room temperature and is insoluble in water. Although it is considered to be insoluble in water, cuprous oxide will dissociate very slowly over time in the presence of saltwater. Based on the fact that this chemical is a solid and the vapor pressure that has been identified is negligible, it is not expected to vaporize at room temperature (ChemIDplus 2014; HSDB 2003; Almeida et al. 2007).

Table 1: Physical and Chemical Properties of Cuprous Oxide (CAS #1317-39-1)

Property	Value	Reference
Molecular formula	Cu_2O	ChemIDplus 2014
SMILES Notation	O([Cu])[Cu]	ChemIDplus 2014
Molecular weight	143.091 g/mol	ChemIDplus 2014
Physical state	Solid	HSDB 2003
Appearance	Cubic crystals, ranging in color from red to brown to yellow	HSDB 2003
Melting point	1235°C	HSDB 2003
Vapor pressure	Negligible	HSDB 2003
Water solubility	Insoluble in water	HSDB 2003
Dissociation constant	Not Identified	
Density/specific gravity	6.0 g/cm^3	HSDB 2003
Partition coefficient	Not identified	

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M, or L): L

Cuprous oxide was assigned a score of Low for carcinogenicity based on an animal study using copper sulfate that did not reveal any evidence of carcinogenicity. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when no evidence of carcinogenicity is found in animal studies (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a carcinogen on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as a carcinogen on any screening lists.
- ECHA 2014
  - No data are available regarding the carcinogenicity of cuprous oxide; however, copper sulfate (CAS # not specified) was used as a read-across substance.
    - *Oral*: Copper sulfate was administered to male and female Sprague-Dawley rats seven days per week for 42-44 weeks at doses of 530 or 1600 ppm[8]. The number of animals per group was not identified. Body weights were noticeably affected in the high dose group, with body weights of the control and low dose groups being at least

[8] Conversion of X ppm copper sulfate equivalent to X mg copper sulfate/kg feed
Males: [(X mg copper sulfate/kg feed)*(0.036 kg feed/day)]/0.523 kg bw
530 ppm copper sulfate = 36.5 mg/kg/day copper sulfate; 1600 ppm copper sulfate = 110.1 mg/kg/day copper sulfate
Females: [(X mg copper sulfate/kg feed)*(0.027 kg feed/day)]/0.338 kg bw
530 ppm copper sulfate = 42.3 mg/kg/day copper sulfate; 1600 ppm copper sulfate = 127.8 mg/kg/day copper sulfate

50% higher than those of the high dose group. Organ weights were comparable to controls, with the exception of the stomach weights in females in the high dose group. Gross pathology for the high dose group revealed bronzed kidneys exhibiting sharp demarcation between the cortex and the medulla, bronzed or yellowish livers, hypertrophied ridges between the cardiac and peptic portions of the stomach, occasional ulcers and some blood, and blood mucus in the intestinal tract. Histopathological analysis revealed well-defined abnormalities of a toxic nature in kidneys in the high dose group. Additionally, icteric[9] pigmentation was increased and cytoplasmic staining was abnormal in the high dose group. Testicular degeneration was noted in all male dose groups. The ovaries of the females did not appear to be affected by treatment. The authors concluded that copper sulfate administration resulted in copper toxicity; however, no neoplasms were observed in any dose groups. As a result, the test substance was not considered to be carcinogenic.

Mutagenicity/Genotoxicity (M) Score (H, M, or L): L

Cuprous oxide was assigned a score of Low for mutagenicity/genotoxicity based on negative *in vivo* and *in vitro* genotoxicity assays using copper sulfate pentahydrate. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when mutagenicity/genotoxicity studies are negative (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is not listed as a mutagen/genotoxicant on any authoritative lists.
    - *Screening:* Cuprous oxide is not listed as a mutagen/genotoxicant on any screening lists.
- ECHA 2014
    - No data were available regarding the mutagenicity/genotoxicity of cuprous oxide; however, copper (II) sulfate pentahydrate (CAS #7758-99-8) was used as a read-across substance to evaluate the potential mutagenicity/genotoxicity of cuprous oxide.
        - *In vitro*: An Ames assay was performed according to OECD Guideline 471 using *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537, and TA102 in the presence and absence of metabolic activation; the assay was determined to be negative for mutagenicity.
        - *In vivo*: A micronucleus assay was performed using male and female CD-1 mice. The test substance was administered twice, with the second administration occurring 24 hours after the first. The animals were sacrificed either 24 or 48 hours after the second administration of the test substance. The test substance was determined to be negative for genotoxicity.
        - *In vivo*: An unscheduled DNA synthesis assay was performed according to OECD Guideline 486. Male rats were administered copper sulfate at doses of 632.5 or 2,000 mg/kg via gavage. Approximately 12-14 hours after the administration, the animals were sacrificed, and hepatocytes were harvested and examined for signs of genotoxicity. Based on the results of this study, copper (II) sulfate pentahydrate was not genotoxic.

Reproductive Toxicity (R) Score (H, M, or L): L

Cuprous oxide was assigned a score of Low for reproductive toxicity based on the absence of reproductive effects in a reproductive toxicity study on copper sulfate pentahydrate. GreenScreen®

[9] Of, relating to, or affected with jaundice.

criteria classify chemicals as a Low hazard for reproductive toxicity when no reproductive effects are reported in reproductive toxicity studies (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is not listed as a reproductive toxicant on any authoritative lists.
    - *Screening:* Cuprous oxide is not listed as a reproductive toxicant on any screening lists.
- ECHA 2014
    - No data were available regarding the reproductive toxicity of cuprous oxide; however, copper sulfate pentahydrate (CAS #7758-99-8) was used as a surrogate to evaluate the toxicity of cuprous oxide.
        - A two-generation reproductive toxicity study was performed according OECD Guideline 416 to evaluate the reproductive toxicity of copper sulfate. Male and female Crl:CD rats (n=30/sex/dose) were exposed to doses of 0, 100, 500, 1,000, and 1,500 ppm copper sulfate[10] daily for 70 days. Following exposure, they were cohoused for mating; this was designated as day 1 of cohabitation. The day on which evidence of mating was observed was designated as day 0 of gestation. Once evidence of mating was observed or two weeks had passed, the animals were separated. Clinical observations were performed at least once daily; any rats found to be moribund were sacrificed. Body weights and food consumption were evaluated throughout the study. The estrous cycle and sperm parameters[11] of the parental generation, in addition to reproductive performance[12], were evaluated in order to assess reproductive toxicity. Each litter from the P1 generation was evaluated at day 0, 4, 7, and 21 postpartum for number of live and dead pups, body weight and any abnormal behavior or appearance. Some of the offspring from the litters were randomly selected to serve as parents of the F2 generation; the pups that were not selected were sacrificed for evaluation. Organ weights were measured and histopathological evaluation was performed in the P1 generation, the F1 and F2 offspring, and adult F1 offspring (i.e., those animals that were used as parental animals for the production of the F2 generation).

[10] For doses of 0, 100, 500, 1,000, and 1,500 ppm, the following dose equivalents for copper were provided by the authors and the following to dose equivalents for cuprous oxide were calculated by ToxServices:
P1 males during premating: 0, 1.53, 7.7, 15.2, and 23.6 mg/kg/day copper; equivalent to 0, 1.72, 8.67, 17.11, and 26.57 mg/kg/day copper oxide
P1 females during premating: 0, 1.92, 9.6, 19.1, and 29.5 mg/kg/day copper; equivalent to 0, 2.16, 10.81, 21.5, and 33.21 mg/kg/day copper oxide
P1 females during gestation: 0, 1.67, 8.6, 17.0, and 26.2 mg/kg/day copper; equivalent to 0, 1.88, 9.68, 19.14, and 29.50 mg/kg/day copper oxide
P1 females during the first 2 weeks of lactation: 0, 3.39, 17.7, 33.8, and 55.7 mg/kg/day copper; equivalent to 0, 3.82, 19.93, 38.05, and 62.71 mg/kg/day copper oxide
F1 males during premating: 0, 2.25, 11.5, 23.5, and 36.1 mg/kg/day copper; equivalent to 0, 2.53, 12.95, 26.46, and 40.64 mg/kg/day copper oxide
F1 females during premating: 0, 2.65, 13.3, 26.7, and 43.8 mg/kg/day copper; equivalent to 0, 2.98, 14.97, 30.06, and 49.31 mg/kg/day copper oxide
F1 females during gestation: 0, 1.69, 8.5, 17.1, and 26.5 mg/kg/day copper; equivalent to 0, 1.90, 9.57, 19.25, and 29.83 mg/kg/day copper oxide
F1 females during the first 2 weeks of lactation: 0, 3.27, 17.6, 35.2, and 55.4 mg/kg/day copper; equivalent to 0, 3.68, 19.81, 39.63, and 62.37 mg/kg/day copper oxide
The equation used to convert copper to cuprous oxide was as follows:
X mg/kg copper * (g copper/1000 mg copper) * (mol copper/63.55 g copper) * (mol cuprous oxide/2 mol copper) * (143.09 g cuprous oxide/mol cuprous oxide) * (1000 mg cuprous oxide/g cuprous oxide) = Y mg/kg cuprous oxide
[11] Parameters measured were sperm motility, morphology, epididymal sperm or testicular spermatid numbers at any dose level.
[12] Parameters measured were precoital interval length, mating, fertility, gestation length, number of implantation sites, or implantation efficiency.

No clinical effects or effects on body weight and food consumption in the P1 generation were observed. Additionally, no effects were observed on estrous cycle, sperm parameters, or reproductive performance. No effects were observed during gross pathological and histopathological examinations in the parental animals; however, organ weights were affected. Specifically, P1 female adult rats had a small but statistically significant decrease in the mean spleen weight in the 1500 ppm (29.5 mg/kg/day) dose group.
No clinical effects or effects on body weight were observed in the F1 generation (in either adults or weanlings), and no reproductive effects were observed in the F1 adults. No findings were reported in gross pathology and histopathology evaluations in any of the F1 generation; however, the F1 weanling rats also had a small but significant decrease in the mean spleen weight at 1500 ppm (36.1 and 43.8 mg/kg/day for males and females, respectively). The spleen weight decrease was not observed in the F1 adults.
No clinical effects or effects on body weight were observed in the F2 offspring. Additionally, no differences in litter size, sex ratio or pup survival differences were observed in the F2 offspring. No findings were reported in gross pathology and histopathology evaluations; however, the F2 weanling rats had a small but significant decrease in the mean spleen weight at 1500 ppm (the dose was not calculated for the weanlings, as they never received the diet with test substance, rather it is the dose of the parental generation from which the weanlings were born). As a result, the LOAELs for reproductive toxicity are as follows: >1500 ppm (23.6 mg/kg/day) for P1 males; >1500 ppm (29.5 mg/kg/day) for P1 females; >1500 ppm (36.1 mg/kg/day) for F1 males; >1500 ppm (43.8 mg/kg/day) for F1 females. It should be noted that the authors did establish the following LOAELs based on decreased spleen weights: 1500 ppm (29.5 mg/kg/day) for P1 females; 1500 ppm (36.1 mg/kg/day) for F1 males; 1500 ppm (43.8 mg/kg/day) for F1 females; 1500 ppm for F2 males; and 1500 ppm for F2 females. As decreased spleen weight is a systemic rather than reproductive effect, it was not used to determine the LOAEL for this endpoint.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M, or L): M
Cuprous oxide was assigned a score of Moderate for developmental toxicity based on developmental effects observed in animal studies on copper hydroxide, which results in categorization as a GHS Reproductive[13] Toxicant Category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when they are categorized as GHS Category 2 Reproductive Toxicants (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is not listed as a developmental toxicant on any authoritative lists.
    - *Screening:* Cuprous oxide is not listed as a developmental toxicant on any screening lists.
- ECHA 2014
    - No data were available regarding the developmental toxicity of cuprous oxide; however, copper hydroxide (CAS #1344-69-0) was used as a surrogate to evaluate the toxicity of cuprous oxide.
        - Copper hydroxide was administered to New Zealand White rabbits via gavage at

[13] The GHS Reproductive Toxicity Category includes Developmental Toxicity.

doses of 0, 7.5, 15, or 30 mg/kg/day copper[14] from days 7 to 28 of gestation. All animals were sacrificed on day 29. Five females were used in the control group, 8 females were used in the 7.5 and 30 mg/kg dose groups, and 9 females were used in the 15 mg/kg dose group. Body weights and food consumption were measured daily, and clinical signs were also recorded daily. Gross pathology and histopathology evaluations were performed on all animals. Additionally, gravid uterine weight, number of corpora lutea, and number of implantations were measured along with the number of live and dead fetuses, the number of resorptions, fetal weight, sex ratio, and external alterations.
Maternal toxicity was observed. Specifically, diarrhea was observed at all dose levels. The incidence was low; however, it was considered to be treatment-related. Additionally, mortality was reported in the high dose, as one rabbit was sacrificed in extremis[15] on day 9 of gestation and another was found dead on day 26 of gestation. Histopathology of the animal that was sacrificed on day 9 revealed that the cause of death was related to a hemolytic event that caused hemoglobin nephropathy and renal failure. Stomach hemorrhages or a small liver that was moderately autolysed was revealed at gross necropsy; however, the study did not identify whether this was observed in one or both of the animals that died early, or if it was a general finding in all treated animals. Embryotoxic and teratogenic effects were also observed in this study. Mean fetal weights were reduced in the high dose group. Additionally, fetal resorptions were slightly increased in the high dose group. Omphalocele[16] was also observed in four of the fetuses in the high dose group. Developmental toxicity was not observed in any other dose group. Anasarca[17], domed head and a short tail was observed in one fetus in the low dose group; however, the authors did not consider these effects to be substance related. No information regarding the statistical significance of any of the aforementioned effects was provided.
Based on the effects observed in this study, the authors established a NOAEL of 7.5 mg/kg/day (8.44 mg/kg/day cuprous oxide) for maternal toxicity and a NOAEL for developmental toxicity of 15 mg/kg/day copper (16.89 mg/kg/day cuprous oxide). Therefore, the LOAELs for maternal toxicity were 15 mg/kg/day copper (16.89 mg/kg/day cuprous oxide) and 30 mg/kg/day copper (33.77 mg/kg/day cuprous oxide) for developmental toxicity. The LOAEL for maternal toxicity was based on mortality, gastric ulcer, hemolytic anemia, and renal damage observed at 30 mg/kg/day copper, and reduced food consumption and reduced body weights at both 15 and 30 mg/kg/day copper. The LOAEL for developmental toxicity was based on reduced mean fetal weights, a slight increase in resorptions, and increased malformations in the high dose group. Based on the results of this study, this chemical is assigned to GHS Reproductive Toxicity Category 2.

- A developmental toxicity study was performed according to OECD Guideline 414 to evaluate the developmental toxicity of copper hydroxide. Copper hydroxide was administered to pregnant New Zealand White rabbits via gavage at doses of 0, 6, 9,

[14] Equivalent to 0, 8.44, 16.89, and 33.77 mg/kg/day cuprous oxide, respectively.
The equation used to convert copper to cuprous oxide was as follows:
X mg/kg copper * (g copper/1000 mg copper) * (mol copper/63.55 g copper) * (mol cuprous oxide/2 mol copper) * (143.09 g cuprous oxide/mol cuprous oxide) * (1000 mg cuprous oxide/g cuprous oxide) = Y mg/kg cuprous oxide
[15] At the point of death.
[16] Protrusion of intestines at the umbilicus.
[17] Extreme generalized edema.

or 18 mg/kg/day copper[18] (n=22/group) from day 7 to 28 of gestation. Animals were sacrificed on day 29. Body weights and food consumption were measured daily, and clinical signs were also recorded daily. Gross pathology and histopathology evaluations were performed on all animals. Additionally, gravid uterine weight, number of corpora lutea, and number of implantations were measured along with litter size, the number of live and dead fetuses, fetal weight, sex ratio, external alterations, and retarded renal development. Skeletal and soft tissue analyses were also performed.

In the high dose group, three animals were found dead during the study. Diarrhea, cageboard-staining, weakness, and irregular respiration before death were observed in one animal. Additionally, stomach hemorrhage and/or ulceration, dark discoloration or mottling of lung tissue, pale liver, gelatinous tan rectal discharge, and brown liquid in the chest cavity were observed in all three animals. Two other females in the high dose group aborted. In the two animals that aborted, one animal had diarrhea and the other had red discolored stomach lining at necropsy. No mortality occurred in the mid and low dose levels. Diarrhea was observed in all dose groups. Body weights, body weight changes, and food consumption were statistically significantly reduced in the mid and high dose groups. Additionally, marked decreases in food consumption and body weight loss were observed during the first week of dosing.

Maternal administration of the test substance did not affect the number of fetuses per litter or the number of early and late embryonic deaths. Mean fetal weight was slightly lower in the high dose group. Although it was not significant, the authors considered it to be substance-related. Spontaneous malformations were observed in four fetuses. In the control group, one fetus showed fused ribs. In the low dose group, one fetus had ectopic kidney[19]. In the high dose group, two fetuses had hemivertebra[20]. All aforementioned malformations were considered to be spontaneous and not treatment-related. Other effects were considered to be treatment-related. In the high dose group, a slight increase in incidence of retarded ossification of the skull and pelvic bones was observed. The skull ossification was statistically significant but the pelvic ossification was not; however, there was a dose response with both effects. No correlation was found with fetal weight. Therefore, the biological relevance of the retarded ossification was not clear. A very high incidence of rib alterations occurred in all dose groups, but was only statistically significant in the high dose group. The authors of this study were unclear as to whether this was biologically significant.

Based on the maternal weight loss and reduced food consumption observed in this study, the authors established a NOAEL and LOAEL of 6 mg/kg/day (6.75 mg/kg/day copper oxide) and 9 mg/kg/day copper (10.13 mg/kg/day copper oxide), respectively, for maternal toxicity. Additionally, based on increased skeletal variations in fetuses, the authors established a NOAEL for developmental toxicity of 6 mg/kg/day copper (6.75 mg/kg/day copper oxide). Therefore, the LOAEL for developmental toxicity was 9 mg/kg/day copper (10.13 mg/kg/day copper oxide).

[18] Equivalent to 0, 6.75, 10.13, and 20.26 mg/kg/day cuprous oxide.
The equation used to convert copper to cuprous oxide was as follows:
X mg/kg copper * (g copper/1000 mg copper) * (mol copper/63.55 g copper) * (mol cuprous oxide/2 mol copper) * (143.09 g cuprous oxide/mol cuprous oxide) * (1000 mg cuprous oxide/g cuprous oxide) = Y mg/kg cuprous oxide
[19] Condition where the kidney is located above, below or on the opposite side of where it normally develops.
[20] Condition where half of a vertebra does not form.

- Based on the results of these studies, cuprous oxide is associated with adverse effects on development. Chemicals that produce developmental effects in animal studies are assigned to GHS Category 2 for Reproductive Toxicity.

Endocrine Activity (E) Score (H, M, or L): DG
Cuprous oxide was assigned a score of Data Gap for endocrine disruption as no data were available regarding the endocrine activity of cuprous oxide. GreenScreen® criteria classify chemicals as a Data Gap for endocrine disruption when no data are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as an endocrine active chemical on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as an endocrine active chemical on any screening lists.
- Not listed as a potential endocrine disruptor on the EU Priority List of Suspected Endocrine Disruptors.
- Not listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
- No data were available regarding the endocrine activity of cuprous oxide.

Group II and II* Human Health Effects (Group II and II* Human)
Note: Group II and Group II* endpoints are distinguished in the v 1.2 Benchmark system. For Systemic Toxicity and Neurotoxicity, Group II and II* are considered sub-endpoints and test data for single or repeated exposures may be used. If data exist for single OR repeated exposures, then the endpoint is not considered a data gap. If data are available for both single and repeated exposures, then the more conservative value is used.

Acute Mammalian Toxicity (AT) Group II Score (vH, H, M, or L): M
Cuprous oxide was assigned a score of Moderate for acute toxicity based on oral toxicity values ranging from 470 to <2,000 mg/kg for cuprous oxide. GreenScreen® criteria classify chemicals as a Moderate hazard for acute toxicity when acute oral toxicity values range from >300 to 2,000 mg/kg (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is listed as "R22: Harmful if swallowed" in the CLP Regulation. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate or high hazard for acute toxicity.
  - *Authoritative:* Cuprous oxide is listed as "H302 Harmful if swallowed" in the CLP Regulation. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate hazard for acute toxicity.
  - *Screening:* Cuprous oxide is listed as "Class D1B" in the WHMIS classifications. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate, high, or very high hazard for acute toxicity.
  - *Screening:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "6.1D (inhalation) – acutely toxic" chemical via inhalation. A GHS-New Zealand 6.1D Acute Toxicity (inhalation) chemical is equivalent to a GHS Category 4 Acute Toxicant. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate hazard for acute toxicity.
  - *Screening:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "6.1D (oral) – acutely toxic" chemical via the oral route. A GHS-New Zealand 6.1D Acute Toxicity (oral) chemical is equivalent to a GHS Category 4 Acute Toxicant. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate hazard for acute

toxicity.

- ChemIDplus 2014
  - An oral LD_{50} of 470 mg/kg cuprous oxide was determined in rats.
- ECHA 2014
  - An oral LD_{50} between 928 and 2,000 mg/kg cuprous oxide was determined in rats.
  - A dermal LD_{50} greater than 2,000 mg/kg cuprous oxide was determined in rats.

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
***Group II Score (single dose)* (vH, H, M, or L):** DG
Cuprous oxide was assigned a score of Data Gap for systemic toxicity (single dose) as no data were available regarding the systemic toxicity/organ effects including immunotoxicity (single dose) of cuprous oxide. GreenScreen® criteria classify chemicals as a Data for systemic toxicity (single dose) when no data are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a systemic toxicant (single exposure) on any authoritative lists.
  - *Screening:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "6.9B (inhalation) – Harmful to target organs or systems" chemical via inhalation. A GHS-New Zealand 6.9B chemical is equivalent to a GHS Category 2 Systemic Toxicant – Repeated Exposure Chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate hazard for systemic toxicity (repeated exposure). It should be noted that the 6.9B categorization does not differentiate between single and repeated exposure. Therefore, this screening list result is included in the list output for both single and repeated dose systemic toxicity; however, a hazard rating could not be assigned based on this list due to insufficient data being available to determine if the 6.9B categorization is for single or repeated exposure for systemic toxicity.
- No data regarding systemic toxicity – single exposure were identified.

***Group II* Score (repeated dose)* (H, M, or L): M**
Cuprous oxide was assigned a score of Moderate for systemic toxicity (repeated dose) as cuprous oxide is designated as a GHS Category 2 Repeated Dose Toxicant based on systemic toxicity studies on copper sulfate pentahydrate. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (repeated dose) when chemicals are GHS Category 2 Repeated Dose Toxicants (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a systemic toxicant (repeated exposure) on any authoritative lists.
  - *Screening:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "6.9B (inhalation) – Harmful to target organs or systems" chemical via inhalation. A GHS-New Zealand 6.9B chemical is equivalent to a GHS Category 2 Systemic Toxicant – Repeated Exposure Chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate hazard for systemic toxicity (repeated exposure). It should be noted that the 6.9B categorization does not differentiate between single and repeated exposure. Therefore, this screening list result is included in the list output for both single and repeated dose systemic toxicity; however, a hazard rating could not be assigned based on this list due to insufficient data being available to determine if the 6.9B categorization is for single or repeated exposure for systemic toxicity.
  - *Screening:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as

a "6.9B (oral) – Harmful to target organs or systems" chemical via oral exposure. Although the 6.9B categorization does not differentiate between single and repeated exposure, the data upon which this categorization is based are for repeated exposure. A GHS-New Zealand 6.9B Systemic Toxicity – Repeated Exposure chemical is equivalent to a GHS Category 2 Systemic Toxicant – Repeated Exposure chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a moderate hazard for systemic toxicity (repeated exposure).

- ECHA 2014
  - No data were available regarding the reproductive toxicity of cuprous oxide; however, copper sulfate pentahydrate (CAS #7758-99-8) was used as a surrogate to evaluate the toxicity of cuprous oxide.
    - Copper sulfate was administered to male and female B6C3F1 mice (n=10/sex/group) at doses of 0, 1,000, 2,000, 4,000, 8,000, and 16,000 ppm[21] in feed seven days per week for 92 days. No clinical signs or mortalities were observed; however, body weight was decreased in a dose-related manner. Body weights and body weight gains were decreased in the 4,000, 8,000, and 16,000 ppm dose groups; however, the decrease was only significant in the top two doses. The heart and kidney of the males in the 16,000 ppm dose group were significantly decreased, and the thymus and kidney of the females in the 16,000 ppm dose group were significantly decreased. Absolute liver weights were decreased in males and females; this was a dose-related decrease, but the decreases were only statistically significant in the 8,000 and 16,000 ppm dose groups in both sexes and the 4,000 ppm dose group in males. Relative organ weights for all dosed animals were generally greater than that of the controls, with several increases being significantly higher than the control groups; however, those organs and dose groups were not specified by the authors. In the higher dose groups, the changes in the absolute and relative organ weights were attributed to the lower final mean weights. Lesions were observed in the forestomach of seven male and four female mice in the high dose group. Histopathological analysis revealed minimal to mild squamous cell hyperplasia with hyperkeratosis of the forestomach of the mucosa at the site of the limiting ridge, and was found in males and females receiving 4,000 ppm copper sulfate or greater. The livers and kidney of male mice in all dose groups and females in the high dose and control groups were stained to determine if copper was present in those organs. Liver cells in the high dose males and females were the only groups that had positive detections for copper; however, even those dose groups had minimal amounts of copper in the stained samples. No copper was detected in the kidneys of any of the groups evaluated for the presence of copper. Based on statistically significant decreased liver weights in males receiving the 4,000 ppm dose and higher and toxicity in the stomach in the 4,000 ppm dose group in both sexes, the authors identified a LOAEL of 2,000 ppm (109.2 mg/kg/day cuprous oxide and 141.9

[21] For doses of 0, 1,000, 2,000, 4,000, 8,000, and 16,000 ppm, the following dose equivalents for copper were provided by the authors and cuprous oxide dose equivalents were calculated by ToxServices:
Males: 0, 44, 97, 187, 398, and 815 mg/kg/day copper, which is equivalent to 0, 49.5, 109.2, 210.5, 448.1, and 917.5 mg/kg/day cuprous oxide, respectively.
Females: 0, 52, 126 267, 536, and 1,058 mg/kg/day copper, which is equivalent to 0, 58.5, 141.9, 300.6, 603.4, and 1191.1 mg/kg/day cuprous oxide, respectively.
The equation used to convert copper to cuprous oxide was as follows:
X mg/kg copper * (g copper/1000 mg copper) * (mol copper/63.55 g copper) * (mol cuprous oxide/2 mol copper) * (143.09 g cuprous oxide/mol cuprous oxide) * (1000 mg cuprous oxide/g cuprous oxide) = Y mg/kg cuprous oxide

mg/kg/day cuprous oxide for males and females, respectively) and a NOAEL of 1,000 ppm (49.5 mg/kg/day cuprous oxide and 58.5 mg/kg/day cuprous oxide for males and females, respectively).

- Copper sulfate was administered to male and female F344/N rats daily in the diet at doses of 0, 500, 1,000, 2,000, 4,000, or 8,000 ppm[22] for 92 days. No clinical signs were observed and no mortality occurred with the exception of one female animal that was accidentally killed. In the 500, 4,000, and 8,000 ppm groups for males and the 8,000 ppm group in females, the final mean body weights were lower than the controls. Food consumption in the high dose groups of both sexes was lower than the controls.

  Hematological effects were observed throughout the study, including significant increases in hematocrit and hemoglobin in both sexes, predominantly in the two highest dose groups. However, these two parameters were significantly decreased as the study progressed. Red blood cell counts were significantly increased in both sexes in the higher dose groups, but, by the end of the study, the increases were only significant in males. Significant decreases in reticulocyte counts were observed in both sexes in the beginning of the study; however, by the end of the study, the counts were significantly increased. Decreases were also observed in the number of nucleated red blood cells, mean cell volume, mean cell hematocrit, primarily in the two highest dose groups in both sexes; however, in some instances, these decreases were also noted in the 2,000 ppm dose group. Mean cell hemoglobin concentrations were significantly increased in both sexes in the higher dose groups. The platelet, leukocyte, and lymphocyte counts as well as the number of segmented neutrophils were also significantly increased, primarily in the 2,000 ppm and greater dose groups.

  The two highest dose groups in males and females also had significant changes in clinical chemistry (i.e., changes in alanine aminotransferase, alkaline phosphate activity, sorbitol dehydrogenase, 5'necleotidase, bile salt). Total protein was significantly decreased in both sexes at least one time point (i.e., day 5, 21, and/or 92) in the 2,000 and greater dose ranges. Albumin was also decreased at various time points throughout the study in both sexes receiving the 2,000 ppm dose and above. Additionally, urea nitrogen was significantly increased for both sexes in the 2,000, 4,000, and 8,000 ppm dose groups at various time points throughout the study. Increased creatinine was reported in high dose females at the end of the study (i.e., day 92). Urinalysis changes were observed throughout the study as well, including significant increases in urinary aspirate aminotransferase (AST) activity and N-acetyl-B-D-glucosaminidase activity. Glucose output was increased in males, but not in females. A decrease in protein output was also noted in high dose males, and, by the end of the study, it was increased in the two highest dose groups. No changes in glucose or protein output were observed in females.

  Males in the high dose group had significant decreases in absolute brain, heart, kidney, liver, lung, and thymus weights, and females in the high dose group had

[22] For doses of 0, 500, 1000, 2000, 4000, and 8000 ppm, the following dose equivalents for copper were provided by the authors and cuprous oxide dose equivalents were calculated by ToxServices:
Males and females: 0, 8, 17, 34, 67, or 138 mg/kg/day copper, which is equivalent to 0, 9.01, 19.14, 38.28, 75.43, and 155.36 mg/kg/day cuprous oxide, respectively.
The equation used to convert copper to cuprous oxide was as follows:
X mg/kg copper * (g copper/1000 mg copper) * (mol copper/63.55 g copper) * (mol cuprous oxide/2 mol copper) * (143.09 g cuprous oxide/mol cuprous oxide) * (1000 mg cuprous oxide/g cuprous oxide) = Y mg/kg cuprous oxide

significantly decreased absolute kidney weights. In general, relative organ weights were comparable to controls. Both sexes in the dose groups receiving 2,000 ppm or greater had forestomach lesions. A histopathological findings associated with this effect was squamous mucosa hyperplasia, which increased in incidence and severity with dose. No evidence of erosion or ulceration was found. Chronic active inflammation was observed in the liver of both sexes, predominantly in the two highest dose groups. Cytoplasmic changes were present in the kidneys of both sexes at doses of 2,000 ppm and above, and this was considered to be treatment-related. Additionally, droplets were observed in the tubule lumina of some animals; however, these were not significant. Renal tubule cell disruption (i.e., nuclear enlargement in males and degeneration of the epithelium in females) was also observed in some of the animals in the high dose group.

Copper was found to accumulate in the liver and kidney, and this effect was observed in a dose-related manner. This effect was seen by the accumulation of zinc in the same tissues; however, no additional details on the accumulation of zinc were reported. Significant increases in copper levels were also elevated in the plasma and testis of the rats in the 2,000 ppm and greater dose groups. Calcium in the plasma was significantly decreased in the two highest dose groups. Additionally, a significant increase in magnesium was observed in the kidney and plasma of rats receiving the 2,000 ppm dose. The plasma of the high dose group also had a significant increase in magnesium; no details were provided about the magnesium concentration in the 4,000 ppm dose group. Nonneoplastic lesions were evaluated; however, the specific incidences were not reported in the review.

The liver and kidneys of rats were evaluated for the presence of copper by staining. Positive staining in both organs was only observed in the two high dose groups. The spleen was evaluated for the presence of iron. Sections of spleen were stained, and a positive response for iron was only observed in the high dose group. This was also seen in the 2,000 and 4,000 ppm dose group; however, it was not as pronounced. The authors did not state why they analyzed the spleen for iron and not copper presence. Reproductive evaluations were performed through sperm morphology analysis and vaginal cytology evaluation; however, the results of these effects were not included in the study. The authors only stated that there were no significant findings in either sex.

The authors identified a LOAEL of 2,000 ppm (equivalent to 34 mg/kg/day copper; 38.28 mg/kg/day cuprous oxide) for males based on forestomach lesions and liver damage. This resulted in a NOAEL of 1,000 ppm (17 mg/kg/day copper; 19.14 mg/kg/day cuprous oxide). A LOAEL of 2,000 ppm (equivalent to 34 mg/kg/day copper; 38.28 mg/kg/day cuprous oxide) was identified for females based on forestomach lesions only. This resulted in a NOAEL of 1,000 ppm (17 mg/kg/day copper; 19.14 mg/kg/day cuprous oxide). It should be noted that kidney damage was observed at 2,000 ppm and 1,000 ppm for males and females, respectively. However, the authors stated that the kidney damage was not considered to be toxicologically relevant, as the effects observed are considered to be specific to the rat. Therefore, that effect was not considered in determining the LOAEL for this study.

Neurotoxicity (N)

***Group II Score (single dose)* (vH, H, M, or L):** DG

Cuprous oxide was assigned a score of Data Gap for neurotoxicity (single dose) as no data were available regarding the neurotoxicity (single dose) of cuprous oxide. GreenScreen® criteria classify chemicals as a Data Gap hazard for neurotoxicity (single dose) when no data are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a neurotoxicant (single exposure) on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as a neurotoxicant (single exposure) on any screening lists.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- No data were identified.

***Group II* Score (repeated dose)* (H, M, or L):** DG

Cuprous oxide was assigned a score of Data Gap for neurotoxicity (repeated dose) as no data were available regarding the systemic toxicity (repeated dose) of cuprous oxide. GreenScreen® criteria classify chemicals as a Data Gap for neurotoxicity (repeated dose) when no data are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a neurotoxicant (repeated exposure) on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as a neurotoxicant (repeated exposure) on any screening lists.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006, 2014).
- No data were identified.

Skin Sensitization (SnS) Group II* Score (H, M, or L): L

Cuprous oxide was assigned a score of Low for skin sensitization based on a guinea pig maximization test that was negative for dermal sensitization for cuprous oxide. GreenScreen® criteria classify chemicals as a Low hazard for skin sensitization when sensitization studies are negative (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a dermal sensitizer on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as a dermal sensitizer on any screening lists.
- ECHA 2014
  - A dermal sensitization study was performed according to OECD Guideline 406 in which the dermal sensitization potential of cuprous oxide was evaluated. Male and female guinea pigs (n=20 /sex) received an induction and challenge application of cuprous oxide. The concentrations used were 0.25% intradermal injection and 50% dermal application for the induction phase. A 50% concentration was used for the dermal challenge phase. No dermal sensitization reactions were observed. Therefore, the authors concluded the test substance was non-sensitizing.

Respiratory Sensitization (SnR) Group II* Score (H, M, or L): DG

Cuprous oxide was assigned a score of Data Gap for respiratory sensitization as no data were available regarding the respiratory sensitization of cuprous oxide. GreenScreen® criteria classify chemicals as a Data Gap for respiratory sensitization when no data are available (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a respiratory sensitizer on any authoritative

lists.
    - *Screening:* Cuprous oxide is not listed as a respiratory sensitizer on any screening lists.
- No data were identified.

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M, or L): L
Cuprous oxide was assigned a score of Low for skin irritation/corrosivity based on a negative dermal irritation study on cuprous oxide. GreenScreen® criteria classify chemicals as a Low hazard for skin irritation/corrosivity when dermal irritation studies are negative for dermal irritation (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is not listed as a skin irritant/corrosive chemical on any authoritative lists.
    - *Screening:* Cuprous oxide is not listed as a skin irritant/corrosive chemical on any screening lists.
- ECHA 2014
    - An acute dermal irritation study was performed according to OECD Guideline 404 to evaluate the dermal irritation of cuprous oxide. Cuprous oxide was applied to the intact and abraded skin of New Zealand White rabbits. Two tests were performed: the first test evaluated the dermal irritation of the test substance as an undiluted paste, and the second test evaluated the dermal irritation of the test substance as a 10% suspension in Tylose. Observations were made 24 and 72 hours after administration. At the 24-hour reading, two animals had slight erythema in the abraded skin; however, the erythema was not observed at the 72-hour mark. Dermal irritation was not observed in the intact skin of any of the rabbits tested. As a result, the authors concluded that test substance was not irritating.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M, or L): *M*
Cuprous oxide was assigned a score of Moderate for eye irritation/corrosivity based on irritating effects observed in several OECD Guideline 405 (eye irritation) studies. GreenScreen® criteria classify chemicals as a Moderate hazard for eye irritation/corrosivity when chemicals are considered to be GHS Category 2 eye irritants (CPA 2012a). Although the studies were not consistent in classifying cuprous oxide as an eye irritant, a moderate hazard rating was assigned based on the irritating effects observed. In order to illustrate the inconsistent results of the studies, the confidence level of the hazard rating was reduced.

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is not listed as an eye irritant/corrosive chemical on any authoritative lists.
    - *Screening:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "Category 6.4A – Irritating to the eye" chemical. A GHS-New Zealand 6.4A Irritating to the eye chemical is equivalent to a GHS Category 2A or 2B Eye Irritant. This translates to a high or moderate hazard score, respectively, for eye irritation/corrosion and a GreenScreen Benchmark Unspecified (LT-U).
- ECHA 2014
    - An eye irritation was performed in accordance with OECD Guideline 405 to evaluate the eye irritation potential of cuprous oxide. 100 mg of cuprous oxide was administered into the left eye of each animal. The right eye remained untreated and served as a control. Of the nine treated animals, three of the animals had their treated eye washed out 30 seconds after treatment. Observations were performed at 1, 24, 48, and 72 hours, as well as 4, 7, 10, 14, and 17 days after treatment. Of the six animals that received long term treatment (i.e., those that did not have their treated eye washed immediately after treatment), no iris lesions were

observed. Conjunctival redness and chemosis was seen in all animals approximately one hour after treatment, but these effects resolved by day four. One animal had grade 1 corneal opacity after 24 hours; however, it resolved by 48 hours. Corneal opacity was observed in a second animal from 24 hours to 14 days, but it resolved by day 17. The authors concluded that while the cuprous oxide has a low potential to induce irritation, the substance was not classifiable as an eye irritant under GHS.

  - An eye irritation study was performed in accordance with OECD Guideline 405 to evaluate the eye irritation potential of cuprous oxide. The test substance was administered to the right eye of each of three animals. The left eye remained untreated to serve as a control. The animals were observed for 21 days after administration. One hour after treatment, all animals had diffused corneal opacities. At 24 hours, translucent opacities had developed in all test animals as well as iritis. By day 14, the opacities had resolved in two of the three animals and by day 7, the iritis had resolved in all three rabbits. In the third animal, the opacities were observed until day 21, as was vascularization. Discoloration of the eye, described by the authors as "a diffuse, beefy red coloration of the conjunctivae", as well as severe swelling of the eye was observed at the 24 hour reading. This effect was reduced over time. By day 7, the swelling and discoloration had resolved in two of the animals, and by day 14, the swelling resolved in the third animal. The authors considered cuprous oxide to be irritating, and they proposed a classification of R36: irritating to eyes.
  - An eye irritation study was performed in accordance with OECD Guideline 405 to evaluate the eye irritation potential of cuprous oxide. The test substance was administered either undiluted to the left eye of each of three animals or diluted as a 10% solution to the left eye of each of three animals (for a total of six individually treated animals). The right eye remained untreated to serve as a control. The animals administered the undiluted test substance were observed for 10 days, and the animals that were administered the 10% solution were observed for 7 days. However, because of specifications to receive the hazard classification of a chemical as an eye irritant under Annex VI of Commission Directive 2001/59/EC, the test substance should be evaluated as an eye irritant undiluted. As a result, the effects were only reported for the animals receiving the undiluted test substance. The mean corneal opacity score was 0. The conjunctivae of the animals were evaluated for redness and chemosis. The average score for redness was 2 over three readings (at 24, 48, and 72 hours). The average score for chemosis for all three animals over three readings was approximately 1.6. The authors concluded that, while cuprous oxide showed slight irritation to the eye, the effects were not sufficient to classify the chemical as an eye irritant.

- While the studies available drew conflicting conclusions as to whether cuprous oxide is irritating to the eye, all studies showed signs of redness and irritation. According to GHS, substances that have the potential to induce reversible eye irritation are considered to be GHS Category 2 eye irritants. Additionally, the GHS-New Zealand classification system identifies cuprous oxide as a GHS Category 2 eye irritant. As a result, the weight of evidence supports a Moderate hazard rating for eye irritation; however, confidence was reduced based on the inconclusive hazard assignments among the OECD Guideline studies.

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M, or L): vH

Cuprous oxide was assigned a score of Very High for acute aquatic toxicity based on measured acute aquatic toxicity values that were less than or equal to 1 mg/L in all three trophospheres using various

copper species. GreenScreen® criteria classify chemicals as a Very High hazard for acute aquatic toxicity when acute aquatic toxicity values are less than or equal to 1 mg/L (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is listed as "H400: Aquatic Acute 1 – Very toxic to aquatic life" in the CLP Regulation. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a Very High hazard score for acute aquatic toxicity.
    - *Authoritative:* Cuprous oxide is listed as "R50/53: Very toxic to aquatic organisms, may cause long term adverse effects in the aquatic environment" in the EU R-Phrases. This translates to a GreenScreen Benchmark Unspecified (LT-U).
    - *Authoritative:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "9.1A (algal) – very ecotoxic in the aquatic environment" chemical. A GHS-New Zealand 9.1A (algal) – very ecotoxic in the aquatic environment chemical is equivalent to a GHS Category 1 Acute Aquatic Toxicant. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a Very High hazard score for acute aquatic toxicity.
    - *Authoritative:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "9.1A (crustacean) – very ecotoxic in the aquatic environment" chemical. A GHS-New Zealand 9.1A (crustacean) – very ecotoxic in the aquatic environment chemical is equivalent to a GHS Category 1 Acute Aquatic Toxicant. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a Very High hazard score for acute aquatic toxicity.
    - *Authoritative:* Cuprous oxide is listed on the New Zealand HSNO/GHS (GHS-New Zealand) as a "9.1A (fish) – very ecotoxic in the aquatic environment" chemical. A GHS-New Zealand 9.1A (fish) – very ecotoxic in the aquatic environment chemical is equivalent to a GHS Category 1 Acute Aquatic Toxicant. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a Very High hazard score for acute aquatic toxicity.
    - *Screening:* Cuprous oxide is listed on the German FEA – Substances Hazardous to Waters (VwVwS) as a "Class 1 Low Hazard to Waters" chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U).
    - *Screening:* Cuprous oxide is listed on the Environment Canada – Domestic Substances List (DSL) as an "inherently toxic in the environment" chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U).
- ECHA 2014
    - No data were available regarding the acute aquatic toxicity of cuprous oxide; however, copper (CAS #7440-50-8) was used as a read-across substance for cuprous oxide.
        - *Fish*: An LC_{50} of 810 µg/L copper (0.810 mg/L copper; 0.912 mg/L cuprous oxide) was determined in fish (*Cyprinus carpio*, 96-hr).
    - No data were available regarding the acute aquatic toxicity of cuprous oxide; however, copper sulfate (CAS #7758-98-7) was used as a read-across substance for cuprous oxide.
        - *Fish*: An LC_{50} of 210 µg/L copper sulfate (0.210 mg/L copper sulfate; 0.094 mg/L cuprous oxide) was determined in fish (*Salmo gairdneri*, 96-hr).
        - *Green Algae*: EbC_{50} values ranged from 15.7-164 µg/L copper sulfate (0.0157-0.164 mg/L copper sulfate; 0.007-0.074 mg/L cuprous oxide) for green algae (*Raphidocelis subcapitata*, 72-hr).
    - No data were available regarding the acute aquatic toxicity of cuprous oxide; however, cupric chloride anhydrous (CAS #7447-39-4) was used as a read-across substance for cuprous oxide.
        - *Aquatic Invertebrate*: An EC_{50} of 9.8 µg/L cupric chloride anhydrous (0.010 mg/L cupric chloride anhydrous; 0.005 mg/L cuprous oxide) was determined in the aquatic invertebrate (*Daphnia magna*, 48-hr).

- No data were available regarding the acute aquatic toxicity of cuprous oxide; however, cupric chloride dihydrate (CAS #10125-13-0) was used as a read-across substance for cuprous oxide.
  - *Green Algae*: A NOEC (72-hr) of 5.7 µg/L cupric chloride dihydrate (0.0057 mg/L cupric chloride dehydrate; 0.0024 mg/L cuprous oxide) was determined in green algae (*Phaeodactylum tricornutum*, 72-hr).

Chronic Aquatic Toxicity (CA) Score (vH, H, M, or L): vH
Cuprous oxide was assigned a score of Very High for chronic aquatic toxicity based on chronic aquatic toxicity values less than or equal to 0.1 mg/L. GreenScreen® criteria classify chemicals as a Very High hazard for chronic aquatic toxicity when aquatic toxicity values are less than or equal to 0.1 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is listed as "H410: Aquatic Chronic 1 – Very toxic to aquatic life with long lasting effects" in the CLP Regulation. This translates to a GreenScreen Benchmark Possible 1 (LT-P1) score.
  - *Screening:* Cuprous oxide is listed on the German FEA – Substances Hazardous to Waters (VwVwS) as a "Class 1 Low Hazard to Waters" chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U).
  - *Screening:* Cuprous oxide is listed on the Environment Canada – Domestic Substances List (DSL) as an "inherently toxic in the environment" chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U).
- ECHA 2014
  - No data were available regarding the acute aquatic toxicity of cuprous oxide; however, copper was used as a read-across substance for cuprous oxide.
    - A NOEC of 13 µg/L for growth rate (as copper sulfate, which is equivalent to 11.7 µg/L cuprous oxide) was determined in the fish (*I. punctatus*, 60-day).
    - A NOEC of 13 µg/L copper (as copper sulfate, which is equivalent to 11.7 µg/L cuprous oxide) for mortality was determined in the fish (*I. punctatus*, 60-day).
    - A NOEC of 7 µg/L copper (as copper sulfate, which is equivalent to 6.28 µg/L cuprous oxide) for growth rate was determined in the fish (*S. fontinalis*, 30-day).
    - A NOEC of 21 µg/L copper (as copper sulfate, which is equivalent to 18.8 µg/L cuprous oxide) for mortality was determined in the fish (*S. fontinalis*, 30-day).
    - A NOEC of 49 µg/L copper (as copper sulfate, which is equivalent to 43.9 µg/L cuprous oxide) for reproduction was determined in the fish (*S. fontinalis*, 30-day).
    - A NOEC of 16 µg/L copper chloride (which is equivalent to 14.3 µg/L cuprous oxide) for growth rate was determined in the fish (*Oncorhynchus mykiss*, 78-day).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): vH
Cuprous oxide was assigned a score of Very High for persistence as it is an inorganic substance, and therefore, recalcitrant. GreenScreen® criteria classify chemicals as a Very High hazard for persistence when chemicals are recalcitrant (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a persistent chemical on any authoritative lists.
  - *Screening:* Cuprous oxide is listed on the German FEA – Substances Hazardous to Waters (VwVwS) as a "Class 1 Low Hazard to Waters" chemical. This translates to a GreenScreen

Benchmark Unspecified (LT-U).
    - *Screening:* Cuprous oxide is listed on the Environment Canada – Domestic Substances List (DSL) as a "DSL substances that are persistent" chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U) and a High or Very High hazard for persistence.
- Degradation is defined as the decomposition of organic molecules to smaller molecules and eventually to carbon dioxide, water, and salts. For inorganic compounds, the concept of degradability as applied to organic compounds has limited or no meaning. Rather the substance may be transformed by normal environmental processes to either increase or decrease the bioavailability of the toxic species. Equally, the log K_{ow} cannot be considered as a measure of the potential to accumulate, and the use of bioaccumulation data should be treated with care (UN 2013). Cuprous oxide is an inorganic substance; therefore, it is recalcitrant.

Bioaccumulation (B) Score (vH, H, M, L, or vL): *M*
Cuprous oxide was assigned a score of Moderate for bioaccumulation, as supported by bioconcentration factors (BCFs) ranging from 0.5 to 617.6. Although some bioconcentration studies reported low BCFs (indication low bioaccumulation potential), other studies revealed higher BCFs, indicating a potential for bioaccumulation. GreenScreen® criteria classify chemicals as a Moderate hazard for bioaccumulation when the most conservative BCF is between 500 and 1,000 (CPA 2012a). Confidence was reduced based on the range of BCFs available in the literature in addition to the fact that bioaccumulation of cuprous oxide is highly dependent on environmental factors, and, therefore, may vary.

- Authoritative and Screening Lists
    - *Authoritative:* Cuprous oxide is not listed as a bioaccumulative chemical on any authoritative lists.
    - *Screening:* Cuprous oxide is listed on the German FEA – Substances Hazardous to Waters (VwVwS) as a "Class 1 Low Hazard to Waters" chemical. This translates to a GreenScreen Benchmark Unspecified (LT-U).
- ECHA 2014
    - No data were available regarding the bioaccumulation of cuprous oxide; however, copper sulfate (CAS Number not specified) was used as a surrogate to evaluate the toxicity of cuprous oxide.
        - *Daphnia magna* were administered copper in the form of copper sulfate for seven days. A bioconcentration factor of 0.5 was determined based on the presence of 70.7 µg copper/g daphnid. No additional details were provided.
        - A variety of species (n=15) of algae were exposed to 34 µg/L for 20-30 days. Following exposure, the algae were harvested, ashed, and analyzed for copper content. Bioconcentration factors ranges from 73.5 to 617.6. No additional details were provided.
    - The bioaccumulation of copper is largely dependent on speciation and environmental conditions (Jorgensen 2010; Di Giulio and Hinton 2008).
- Limited data are available to assess the bioaccumulation potential of cuprous oxide; however, it is known that many environmental conditions play a role in the bioavailability, and therefore, the bioaccumulation of copper. Although some studies indicate that copper has low bioaccumulation, as illustrated by low bioconcentration factors, other studies have revealed that, in certain environmental conditions, copper does have the potential to bioaccumulate, as supported by larger bioconcentration factors (ECHA, 2014; DiGiulio and Hinton, 2008; Jorgensen, 2010). As a result, the bioaccumulation of copper is considered to be moderate, based on some evidence of copper being bioaccumulative in certain environmental conditions. However, confidence is reduced based on the

wide range of bioconcentration factors reported in the literature, as well as the major role environmental conditions play in the bioavailability of cuprous oxide.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M, or L): *L*
Cuprous oxide was assigned a score of Low for reactivity based on an HMIS and NFPA Rating of 0 for reactivity. Confidence level was reduced due to lack of experimental data. GreenScreen® criteria classify chemicals as a Low hazard for reactivity when a chemical is not classifiable under GHS as a reactive chemical (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a reactive chemical on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as a reactive chemical on any screening lists.
- ESIS 2000
  - Not explosive. No additional details were provided.
  - Not oxidizing. No additional details were provided.
- Sigma-Aldrich 2014; ScienceLab.com 2013
  - Cuprous oxide has an HMIS and NFPA Rating of 0 for reactivity.

Flammability (F) Score (vH, H, M, or L): *L*
Cuprous oxide was assigned a score of Low for flammability based on an HMIS and NFPA Rating of 0 for flammability. Confidence level was reduced due to lack of experimental data. GreenScreen® criteria classify chemicals as a Low hazard for flammability when a chemical is not classifiable under GHS as a flammable chemical (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Cuprous oxide is not listed as a flammable chemical on any authoritative lists.
  - *Screening:* Cuprous oxide is not listed as a flammable chemical on any screening lists.
- ESIS 2000
  - Not flammable. No additional details were provided.
- Sigma-Aldrich 2014; ScienceLab.com 2013
  - Cuprous oxide has an HMIS and NFPA Rating of 0 for flammability.

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APPENDIX A: Hazard Benchmark Acronyms
(in alphabetical order)

(AA) Acute Aquatic Toxicity

(AT) Acute Mammalian Toxicity

(B) Bioaccumulation

(C) Carcinogenicity

(CA) Chronic Aquatic Toxicity

(D) Developmental Toxicity

(E) Endocrine Activity

(F) Flammability

(IrE) Eye Irritation/Corrosivity

(IrS) Skin Irritation/Corrosivity

(M) Mutagenicity and Genotoxicity

(N) Neurotoxicity

(P) Persistence

(R) Reproductive Toxicity

(Rx) Reactivity

(SnS) Sensitization- Skin

(SnR) Sensitization- Respiratory

(ST) Systemic/Organ Toxicity

APPENDIX B: Results of Automated GreenScreen® Score Calculation for Cuprous Oxide (CAS #1317-39-1)

GreenScreen® Score Inspector

Table 1: Hazard Table

			Group I Human					Group II and II* Human								Ecotox		Fate		Physical	
			Carcinogenicity	Mutagenicity/Genotoxicity	Reproductive Toxicity	Developmental Toxicity	Endocrine Activity	Acute Toxicity	Systemic Toxicity		Neurotoxicity		Skin Sensitization*	Respiratory Sensitization*	Skin Irritation	Eye Irritation	Acute Aquatic Toxicity	Chronic Aquatic Toxicity	Persistence	Bioaccumulation	Reactivity	Flammability
Table 2: Chemical Details									S	R *	S	R *	*	*								
Inorganic Chemical?	**Chemical Name**	**CAS#**	**C**	**M**	**R**	**D**	**E**	**AT**	**STs**	**STr**	**Ns**	**Nr**	**SNS***	**SNR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
Yes	**Cuprous Oxide**	**1317-39-1**	**L**	**L**	**L**	**M**	DG	**M**	DG	**M**	DG	DG	**L**	DG	**L**	*M*	**vH**	**vH**	**vH**	*M*	*L*	*L*

Table 3: Hazard Summary Table

Benchmark	a	b	c	d	e	f	g
1	No	No	Yes	No	No		
2	STOP						
3	STOP						
4	STOP						

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Cuprous Oxide	1

Note: Chemical has not undergone a data gap assessment. Not a Final GreenScreen™ Score

Table 6

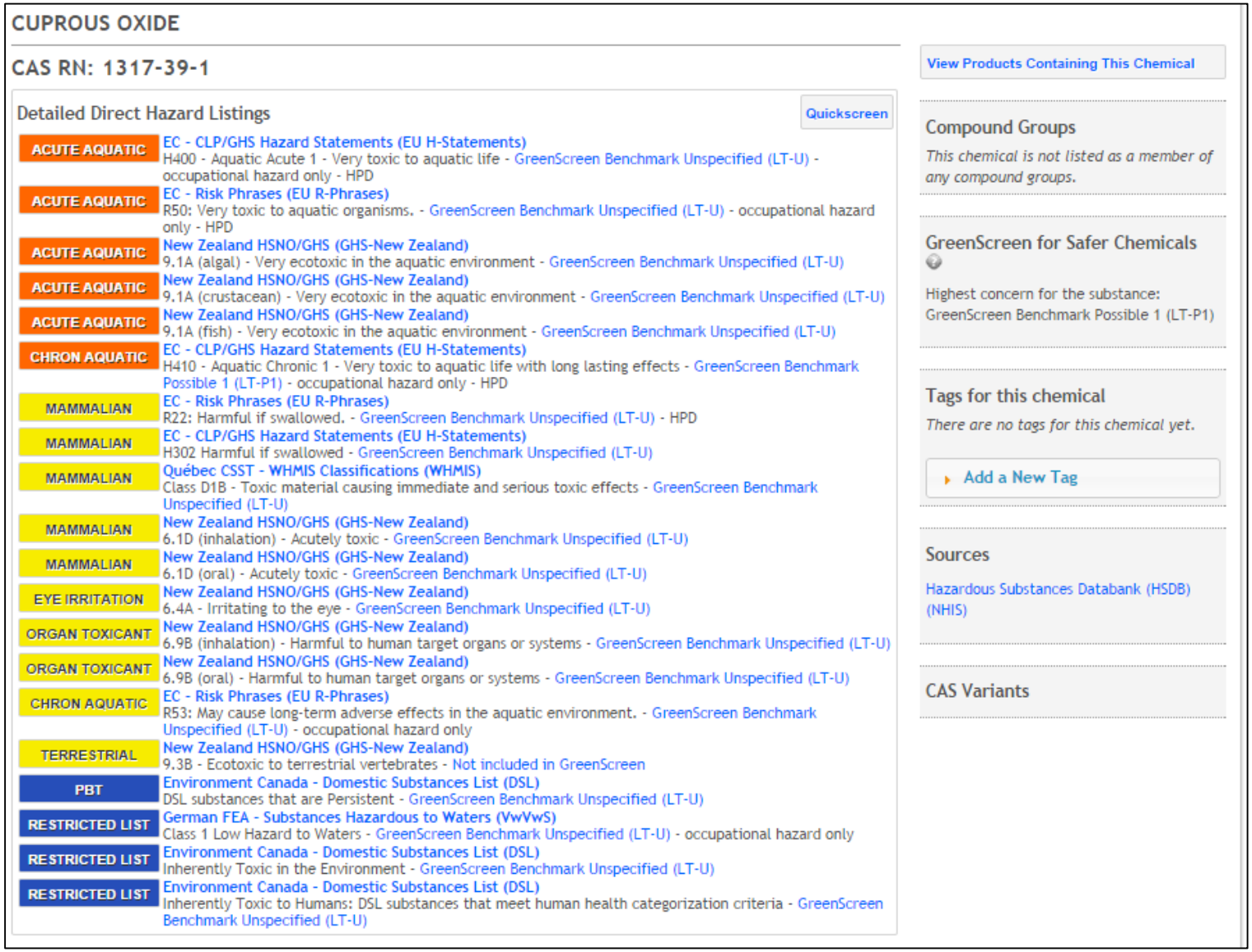
Chemical Name	Final GreenScreen® Benchmark Score
Cuprous Oxide	1

After Data gap Assessment
Note: No Data gap Assessment Done if Preliminary GS Benchmark Score is 1.

Table 5: Data Gap Assessment Table

Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												1
2												
3												
4												

APPENDIX C: Pharos Output for Cuprous Oxide (CAS #1317-39-1)



CUPROUS OXIDE

CAS RN: 1317-39-1

Detailed Direct Hazard Listings — Quickscreen

ACUTE AQUATIC	EC - CLP/GHS Hazard Statements (EU H-Statements) H400 - Aquatic Acute 1 - Very toxic to aquatic life - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only - HPD
ACUTE AQUATIC	EC - Risk Phrases (EU R-Phrases) R50: Very toxic to aquatic organisms. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only - HPD
ACUTE AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1A (algal) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
ACUTE AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1A (crustacean) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
ACUTE AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1A (fish) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	EC - CLP/GHS Hazard Statements (EU H-Statements) H410 - Aquatic Chronic 1 - Very toxic to aquatic life with long lasting effects - GreenScreen Benchmark Possible 1 (LT-P1) - occupational hazard only - HPD
MAMMALIAN	EC - Risk Phrases (EU R-Phrases) R22: Harmful if swallowed. - GreenScreen Benchmark Unspecified (LT-U) - HPD
MAMMALIAN	EC - CLP/GHS Hazard Statements (EU H-Statements) H302 Harmful if swallowed - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	Québec CSST - WHMIS Classifications (WHMIS) Class D1B - Toxic material causing immediate and serious toxic effects - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (inhalation) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1D (oral) - Acutely toxic - GreenScreen Benchmark Unspecified (LT-U)
EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye - GreenScreen Benchmark Unspecified (LT-U)
ORGAN TOXICANT	New Zealand HSNO/GHS (GHS-New Zealand) 6.9B (inhalation) - Harmful to human target organs or systems - GreenScreen Benchmark Unspecified (LT-U)
ORGAN TOXICANT	New Zealand HSNO/GHS (GHS-New Zealand) 6.9B (oral) - Harmful to human target organs or systems - GreenScreen Benchmark Unspecified (LT-U)
CHRON AQUATIC	EC - Risk Phrases (EU R-Phrases) R53: May cause long-term adverse effects in the aquatic environment. - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
TERRESTRIAL	New Zealand HSNO/GHS (GHS-New Zealand) 9.3B - Ecotoxic to terrestrial vertebrates - Not included in GreenScreen
PBT	Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent - GreenScreen Benchmark Unspecified (LT-U)
RESTRICTED LIST	German FEA - Substances Hazardous to Waters (VwVwS) Class 1 Low Hazard to Waters - GreenScreen Benchmark Unspecified (LT-U) - occupational hazard only
RESTRICTED LIST	Environment Canada - Domestic Substances List (DSL) Inherently Toxic in the Environment - GreenScreen Benchmark Unspecified (LT-U)
RESTRICTED LIST	Environment Canada - Domestic Substances List (DSL) Inherently Toxic to Humans: DSL substances that meet human health categorization criteria - GreenScreen Benchmark Unspecified (LT-U)

View Products Containing This Chemical

Compound Groups

This chemical is not listed as a member of any compound groups.

GreenScreen for Safer Chemicals

Highest concern for the substance: GreenScreen Benchmark Possible 1 (LT-P1)

Tags for this chemical

There are no tags for this chemical yet.

Add a New Tag

Sources

Hazardous Substances Databank (HSDB) (NHIS)

CAS Variants

Sources to Check for GreenScreen® Hazard Assessment

Note: For a GreenScreen® Hazard Assessment, data queries should be initially limited to the following references. If data gaps exist after these references have been checked, additional references may be utilized.

U.S. EPA High Production Volume Information System (HPVIS):
http://www.epa.gov/hpvis/index.html

UNEP OECD Screening Information Datasets (SIDS):
http://www.chem.unep.ch/irptc/sids/OECDSIDS/sidspub.html

OECD Existing Chemicals Database: http://webnet.oecd.org/hpv/ui/SponsoredChemicals.aspx

European Chemical Substances Information System IUCLID Chemical Data Sheets:
http://esis.jrc.ec.europa.eu/index.php?PGM=dat

National Toxicology Program: http://ntp.niehs.nih.gov/

International Agency for the Research on Cancer:
http://monographs.iarc.fr/ENG/Classification/index.php

Human and Environmental Risk Assessment (HERA) on ingredients of household cleaning products:
http://www.heraproject.com/RiskAssessment.cfm

European Chemicals Agency (ECHA) REACH Dossiers: http://echa.europa.eu/

Licensed GreenScreen® Profilers

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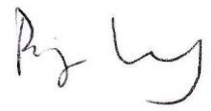

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