Triclosan (CAS# 3380-34-5) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared by:

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GreenScreen® Executive Summary for Triclosan (CAS #3380-34-5)

Triclosan is a nonionic diphenyl ether derivative that is used in cosmetics and toilet soaps as an antiseptic. It has also some bacteriostatic and fungistatic activity.

Triclosan was assigned a GreenScreen® Benchmark Score of 1 ("Avoid: Chemical of High Concern") as it is a PBT chemical due to high persistent (P), high bioaccumulation (B), very high Group II Human Toxicity (acute toxicity (AT) and systemic toxicity single dose (STs)) and very high ecotoxicity (acute aquatic (AA) and chronic aquatic (CA)). This corresponds to GreenScreen® benchmark classification 1a in CPA 2011. Data gaps (DG) exist for endocrine activity (E) 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), triclosan meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if triclosan were assigned a High score for the data gap E, or a Very High score for SnR*, it would still be categorized as a Benchmark 1 Chemical.

GreenScreen® Benchmark Score for Relevant Route of Exposure:

All exposure routes (oral, dermal and inhalation) were evaluated together, as a standard approach for GreenScreen® evaluations, so the GreenScreen® Benchmark Score of 1 ("Avoid: Chemical of High Concern") assigned to triclosan is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for Triclosan

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	**M**	**R**	**D**	**E**	**AT**	**ST**		**N**		**SnS***	**SnR***	**IrS**	**IrE**	**AA**	**CA**	**P**	**B**	**Rx**	**F**
						single	repeated*	single	repeated*										
L	**L**	**M**	**M**	**M**	**vH**	**vH**	**M**	DG	*M*	**L**	DG	**H**	**H**	**vH**	**vH**	**H**	**H**	**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 Triclosan (CAS #3380-34-5)

GreenScreen® Version 1.2 Draft Assessment
Note: Verification Has Not Been Performed on this GreenScreen® Assessment

Chemical Name: Triclosan

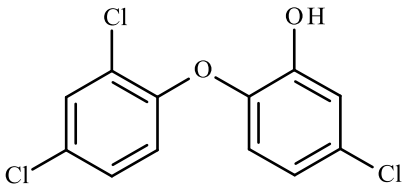
CAS Number: 3380-34-5

GreenScreen® Assessment Prepared By:
Name: Mouna Zachary, Ph.D.
Title: Toxicologist
Organization: ToxServices LLC
Date: January 10, 2014, May 27,2014

Quality Control Performed By:
Name: Dr. Margaret H. Whittaker, Ph.D., M.P.H., CBiol., F.S.B., E.R.T., D.A.B.T.
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: February 7, 2014, May 27, 2014

Confirm application of the *de minimus* rule[1]: Not applicable for triclosan; not a mixture.

Chemical Structure(s):



Triclosan (CAS#3380-34-5)

Also called: 2,4,4'-Trichloro-2'-hydroxy diphenyl ether; Phenol,5-chloro-2-(2,4-dichlorophenoxy)-; CH 3565; Cloxifenolum; Lexol 300; Phenyl ether, 2'-hydroxy-2,4,4'-trichloro; Irgasan DP 300; Triclosanum (ChemIDplus 2014).

Chemical Structure(s) of Chemical Surrogates Used in the GreenScreen®:
No chemical surrogates were sought as the existing data satisfy the data requirement for the assigned benchmark.

Identify Applications/Functional Uses:
1. Antiseptic in cosmetics and toilet soaps at up to 0.3% (ChemIDplus 2014, CIR 2012, SCCS 2011)
2. Preservative for cosmetic and detergent preparations at up to 0.3% (HSDB 2012, CIR 2012, SCCS 2011)
3. In Canada, Triclosan is used as a medicinal ingredient in drug products (0.1 – 1.0% in antiseptic skin cleansers and up to 1% in others) and a non-medicinal ingredient in cosmetics (up to 0.03% in mouthwash and up to 0.3% in others), natural health products and drug

[1] 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

products, as well as a registered pest control product as a material preservative (up to 0.375%) (Environment Canada 2012).

GreenScreen® Summary Rating for Triclosan [2]: Triclosan was assigned a GreenScreen® Benchmark Score of 1 ("Avoid: Chemical of High Concern") as it is a PBT chemical due to high persistent (P), high bioaccumulation (B), very high Group II Human Toxicity (acute toxicity (AT) and systemic toxicity single dose (STs)) and very high ecotoxicity (acute aquatic (AA) and chronic aquatic (CA)). This corresponds to GreenScreen® benchmark classification 1a in CPA 2011. Data gaps (DG) exist for endocrine activity (E) 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), triclosan meets requirements for a GreenScreen® Benchmark Score of 1 despite the hazard data gaps. In a worst-case scenario, if triclosan were assigned a High score for the data gap E, or a Very High score for SnR*, it would still be categorized as a Benchmark 1 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Triclosan

Group I Human					Group II and II* Human									Ecotox		Fate		Physical	
C	M	R	D	E	AT	ST		N		SnS*	SnR*	IrS	IrE	AA	CA	P	B	Rx	F
						single	repeated*	single	repeated*										
L	L	M	M	M	vH	vH	M	DG	M	L	DG	H	H	vH	vH	H	H	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 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[3]

Triclosan is stable to hydrolysis and is persistent under anaerobic conditions. In the environment, triclosan will exist partially in the anionic form at pH values of 5 to 9 and therefore volatilization of the anion from water surfaces is not expected to be an important fate process. Degradation of triclosan in soil incubated under aerobic conditions proceeds primarily via the formation of methyl triclosan and significant amounts of bound residues. Moreover, photolytic degradation of triclosan was experimentally measured in fresh and sea water with half-lives of 8 and 4 days, respectively, with a degradation product of 2,8-

[2] 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.

[3] 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.

dichlorodibenzo-p-dioxin. Based on these degradation scenarios, feasible and relevant transformation products are listed in Table 1, below.

Table 1: Transformation Products of Triclosan

Life Cycle Stage	Transformation Pathway	Transformation Products	CAS #	List Translator Results[4,5]
End of Life	Degradation in soil under aerobic conditions	Methyl triclosan	4640-01-1	Not in Pharos database but classified as Toxic to aquatic life (ECHA 2014a)
End of Life	Photolysis	2,8-Dichlorodibenzo-p-dioxin	38964-22-6	Not in Pharos database

Introduction

Triclosan is a nonionic diphenyl ether derivative. It is a broad spectrum antimicrobial used as an antiseptic, disinfectant or preservative in clinical settings, cosmetics, ousehold cleaning products, plastic materials, toys, paints, medical devices, textiles, kitchen utensils, and so on. In the European Union, 85% of the triclosan produced is used in personal care products, 10% in plastics and food contact materials, and 5% for textiles. Both the European Union and United States have specified the usage limit of 0.3% for triclosan in personal care products (CIR 2012, SCCS 2010, 2011). The European Union banned its use in food-contact plastics and as a food/feed preservative (SCCS 2010). No similar rules are found for the United States.

In Canada, triclosan is used as a medicinal ingredient in drug products (0.1 – 1.0% in antiseptic skin cleansers and up to 1% in others) and a non-medicinal ingredient in cosmetics (up to 0.03% in mouthwash and up to 0.3% in others), natural health products and drug products, as well as a registered pest control product as a material preservative (up to 0.375%). However, as registrants of pesticide products containing triclosan have indicated their intention to discontinue the registration of these products, after the expiry date of December 31, 2014, triclosan will no longer be permitted for use as a pesticide in Canada and cannot be contained in any treated articles imported into Canada unless a new triclosan product is registered in Canada. The Canadian government concluded that triclosan is safe for human health within identified maximum limits, but can be harmful to the environment (Environment Canada 2012, Government of Canada 2012).

ToxServices assessed Triclosan against GreenScreen® Version 1.2 (CPA 2013) following procedures outlined in ToxServices' SOP 1.37 (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

[4] The GreenScreen® List Translator identifies specific authoritative or screening lists that should be searched to screen for GreenScreen® benchmark 1 chemicals (CPA 2012). Pharos (Pharos 2013) is an online list-searching tool that is used to screen chemicals against the lists in the List Translator electronically.
[5] The way transformation products are assessed depends on the Benchmark Score of the parent chemical (See Guidance).

(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 Pharos output indicates benchmark or possible benchmark scores for each human health and environmental endpoint. The output for triclosan can be found in Appendix C and a summary of the results can be found below:

PBT
- Oregon DEQ – Priority Persistent Pollutants Tier 1
- Environment Canada DSL – DSL substances that are persistent

Endocrine
- ChemSec SIN list – Equivalent concern, including endocrine disruption, SIN list 1.0
- TEDX – Potential endocrine disruptor

Acute aquatic
- EC H400 – Very toxic to aquatic life
- EC R50 – Very toxic to aquatic organisms
- GHS New Zealand – 9.1A (algal, crustacean, fish) – Very ecotoxic in the aquatic environment

Chronic aquatic
- EC H410 – Very toxic to aquatic life with long lasting effects
- EC R53 – May cause long-term adverse effects in the aquatic environment

Eye irritation
- EC R36 – Irritating to eyes
- H319 – Causes serious eye irritation
- GHS New Zealand – 6.4A: Irritating to the eye

Skin irritation
- EC R38 – Irritating to skin
- EC H315 – Causes skin irritation
- GHS New Zealand – 6.3A: Irritating to the skin

Terrestrial
- GHS New Zealand – 9.3C: Harmful to terrestrial vertebrates

Mammalian
- GHS New Zealand – 6.1E (Oral): Acutely toxic

Restricted list
- German FEA – Class 2 Hazard to waters
- Hazardous 100 (SCHF) – Chemicals of high concern
- Environment Canada DSL – Inherently toxic in the environment

PhysioChemical Properties of Triclosan

The physiochemical properties of Triclosan are summarized in Table 1. Triclosan is an off-white, odorless, tasteless, crystalline powder with low volatility. It should ionize to some extent at environmentally relevant pH values (i.e., pH 6–9) as indicated by its acid dissociation constant (pKa) of 8.1.

Table 2: Physical and Chemical Properties of Triclosan (CAS #3380-34-5)

Property	Value	Reference
Molecular formula	$C_{12}H_7Cl_3O_2$	ChemIDplus 2014

Table 2: Physical and Chemical Properties of Triclosan (CAS #3380-34-5)		
Property	**Value**	**Reference**
SMILES Notation	c1(Oc2c(cc(Cl)cc2)Cl)c(cc(Cl)cc1)O	ChemIDplus 2014
Molecular weight	289.544	ChemIDplus 2014
Physical state	Crystalline	ECHA 2014b
Appearance	White powder	ECHA 2014b
Melting point	56.4ºC	ECHA 2014b
Vapor pressure	0.0003 Pa at 20ºC	ECHA 2014b
Water solubility	6.5 mg/L at 20ºC and pH 5	ECHA 2014b
Dissociation constant	pKa = 8.14 at 20ºC	ECHA 2014b
Density/specific gravity	1.55 g/cm^3 at 22°C	ECHA 2014b
Partition coefficient (log K_{OW})	4.8 at 25°C and pH 6.7	ECHA 2014b

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

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

Triclosan was assigned a score of Low for carcinogenicity based on no evidence of carcinogenic effects following two-year carcinogenicity study in rats. GreenScreen® criteria classify chemicals as a Low hazard for carcinogenicity when adequate and negative data are available, there are no structural alerts, and they are not GHS-classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- Oral
  - ECHA 2014b
    - In a combined chronic toxicity and carcinogenicity study conducted according to the OECD Guideline 453, Sprague-Dawley rats (60/sex/dose) received triclosan (99% pure) in diet at the doses of 0, 300, 1000, or 3000 ppm for 2 years, and additional groups (20/sex) were given 6000 ppm in their diet for 1 year. Of these groups, 15 animals (sex/dose) were killed after 13, 26 and 78 weeks. No treatment-related tumours, including hepatic tumours, were seen in any of the treated rats examined histologically at 52 or 104 weeks.
    - In an oral carcinogenicity study in hamsters (OECD TG 451), triclosan was administered via the diet to 60 hamsters per sex per dose at 0, 12.25, 75 or 250 mg/kg/day for 90 to 95 weeks. At the highest dose, systemic toxicity was clearly evident in both sexes, and deterioration in the clinical condition and increase in mortality were observed in males after week 80, suggesting that the maximum tolerated dose was exceeded. No treatment related tumours were observed at any dose in either sex. Based on these results, triclosan was considered to have no carcinogenic potential.

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

Triclosan was assigned a score of Low for mutagenicity/genotoxicity based on negative results obtained from *in vitro* and *in vivo* mutagenicity and genotoxicity assays. GreenScreen® criteria classify chemicals as a Low hazard for mutagenicity/genotoxicity when adequate data are available and negative results are seen for both mutagenicity and clastogenicity, there are no structural alerts, and they are not classified under GHS (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- ECHA 2014b
    - A GLP compliant Ames bacterial mutation assay (OECD 471) was conducted utilizing *Salmonella typhimurium* tester strains TA98, TA 100, TA 1535 and TA1537 at concentrations of up to 1.5 µg/plate, in the presence and absence of metabolic activation. No increase in revertants was observed and triclosan was reported as negative for mutagenicity under the tested conditions.
    - In a GLP compliant *in vitro* mammalian cell gene mutation test (OECD 476), triclosan did not induce mutation at the TK +/- locus of L5178 mouse lymphoma cells at concentrations of up to 25 µg/mL in the presence and absence of metabolic activation.
    - Triclosan produced negative results in two unscheduled DNA synthesis assays (OECD 482) in rat primary hepatocytes, when used at concentrations up to 250 µg/mL.
    - Triclosan produced negative results in a gene mutation assay conducted with *Saccharomyces cerevisiae* strain when used at concentrations up to 200 mg/L, without metabolic activation.
    - A GLP compliant *in vitro* mammalian chromosome aberration test (OECD 473) was conducted utilizing Chinese hamster lung fibroblasts (V79) at concentrations of up to 60 µg/mL. Triclosan was found to induce a dose-related increase in the yield of cells with abnormal chromosome morphology at concentrations > 3 µg/mL for 18–28 hours. However, cytotoxicity was observed at these concentrations.
    - No signs of structural chromosomal aberrations were observed in the *in vivo* bone marrow chromosomal aberration test conducted according to the OECD Guideline 475 at the single gavage dose of 4000 mg/kg in male and female Wistar rats.

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

Triclosan was assigned a score of Moderate for reproductive toxicity based on decreased sperm production and histopathological changes in gonads associated with endocrine disruption. GreenScreen® criteria classify chemicals as a Moderate hazard for reproductive toxicity when they are classified to GHS category 2 (suspected) for any route of exposure or there are limited or marginal evidence of reproductive toxicity in animals (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- ECHA 2014b
    - In a GLP compliant 2-generation reproduction toxicity study conducted according

to the EPA OPP 83-4, Sprague-Dawley rats (25/sex/group (F0 generation), 30/sex/group (F1 generation)) received triclosan by daily gavage at doses of 0, 300, 1000, and 3000 ppm. Males and females were exposed 10 weeks before mating, during mating, during pregnancy and during lactation until sacrifice. No treatment-related mortalities or clinical signs were observed. Food consumption and body weight gain were comparable to those in controls. Macroscopic and microscopic examination of the animals did not reveal any changes attributable to treatment. Mating and fertility indices of both sexes, gestation index, mean duration of gestation, and the mean pup body weight were comparable between treated animals and controls. The authors concluded that the treatment did not induce any adverse effects on reproduction in the parental generation (F0 and F1), and the reproductive NOAEL was established at 3000 ppm.

- EC 2009 -
    - In a short-term reproductive toxicity study, male Wistar rats (8/dose) were given triclosan (98% purity, suspended in phosphate buffered saline) by gavage at 0, 5, 10 or 20 mg/kg/day for 60 days. Significant reduction in testes and accessory sex tissues weights were found at 10 and 20 mg/kg/day. There were a decrease of daily sperm production and histopathological changes in the vas deferens and in the prostate at the highest dose. The authors proposed the mechanism of action as antiandrogenic activity of triclosan, which was supported by reduced level of steriodogenic acute regulatory protein (StAR), the activity of testicular steroidogenic enzymes and serum hormone levels. A NOAEL was established at 5 mg/kg/day for this study.
    - The reliability of the above study has been questioned during non-careful writing leading to typos, and the possibility of the effects from impurities. In addition, the significant decrease in testes weights were not seen in a 90-day study in rats at doses of up to 600 mg/kg/day, and these results were not consistent with the two-generation reproduction toxicity study in rats described above. However, sperm counts and viability were not examined in the 2-generation study. Furthermore, weight and histopathology of gonads were not reported in available studies with triclosan of high purity. In light of other studies demonstrating an endocrine disruption effect of triclosan, SCCP concluded that the observations in this study cannot be disregarded.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): M
Triclosan was assigned a score of Moderate for developmental toxicity based on evidence of developmental toxicity (mainly decreased fetal body weights) seen in animal studies. GreenScreen® criteria classify chemicals as a Moderate hazard for developmental toxicity when they are classified to GHS category 2 (suspected) for any route of exposure or there are limited or marginal evidence of developmental toxicity in animals (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- ECHA 2014b
    - In a developmental study conducted in compliance with OECD Guideline 414, timed-pregnant New Zealand White rabbits (18/dose) and Sprague-Dawley rats (24/dose) were administered suspensions of triclosan daily by gavage during gestation days 6 to 18 and 6 to 15, respectively. The doses for both rabbits and

rats were 0, 15, 50, or 150 mg/kg/day. In rabbits, maternal toxicity was observed at the 150 mg/kg dose as indicated by decreased gestation weights during the treatment period; decreased body weight gain over the entire testing period (day 6 to 19 of gestation), and decreased food consumption over the treatment period. No treatment-related external, visceral or skeletal malformations or variations were observed in rabbit fetuses. In rats, slight maternal toxicity (decreased gestation weights, body weight gain and food consumption) was observed at the 150 mg/kg dose and slight retardation in the ossification of the cranium, vertebrae, metacarpals, sternebrae, and pelvic girdle was also observed at this dose. There was no evidence of teratogenicity at any dosage in either species. Based on this, the maternal NOAEL was 50 mg/kg/day for rabbits and rats and the developmental NOAEL was 150 mg/kg/day for rabbits and 50 mg/kg/day for rats.

- In a prenatal developmental toxicity study in rats, triclosan (purity 99.8%) was administered by gavage to pregnant female Sprague-Dawley rats (5 rats per group) on days 6–15 of gestation at a dose level of 5, 10, 25, 50, or75 mg/kg/day. At 75 mg/kg/day, decrease in body weight gain during treatment through gestation was observed only in one animal as weight data for the remaining four animals in the group were within the range of values for the control animals. In addition, fetal weights were also reduced at this dose level. Based on these findings, a maternal and a developmental NOAEL of 50 mg/kg/day was established. There was no evidence of prenatal toxicity or teratogenicity at any dose level in this study; therefore, a teratogenicity NOAEL of 75 mg/kg/day, the highest dose tested, was established.
- In one GLP-compliant range-finding developmental toxicity study in CD-1 mice, pregnant animals (8/group) received triclosan in the diet from gestation day 6 to 15 at doses of 0, 5, 10, 20, 40, 80 or 160 mg/kg/day. At the highest dose, triclosan led to reduced body weight gain and mean body weight in dams. Increased liver weights were reported at 80 and 160 mg/kg/day. Fetal body weight was statistically significantly reduced at doses of 40 mg/kg/day and above. At 160 mg/kg/day, there were increased litter averages for resorption (early and late), percent of resorbed conspectuses and the number of dams with resorptions. Therefore, ECHA established the NOAEL for both maternal toxicity and teratogenicity at 25 mg/kg/day.
- In another developmental toxicity study in mice conducted in compliance with OECD Guideline 414, triclosan (99% pure) was administered via the diet to 25 CD-1 (ICR)BR female mice at a target dose level of 0, 10, 25, 75 or 350 mg/kg/day from day 6 to day 15 of gestation. The maternal toxicity appeared to be minor, with liver weight increases (7% and 17% absolute and relative to brain weight, respectively; statistically significant) and 1 out of 25 dams with a tan-coloured liver at 75 mg/kg bw per day. The NOAEL of 25 mg/kg/day for maternal toxicity was established based on these findings. At 350 mg/kg/day a statistically significant increase of the incidence of variations (characterized as irregular ossification of the phalanges) were noted. Irregular ossification of interfrontal bones (an extra bone between the frontal bones of the skull) was reported at 75 mg/kg/day; however, the biological significance of this finding was unclear, and incidences were within historical control ranges. Fetal weight was decreased by 14% and 18%, respectively, at the 75 and 350 mg/kg/day dose

levels. The decreased fetal body weight at 75 mg/kg/day was considered treatment related, and a developmental NOAEL of 25 mg/kg/day was established.

- In a GLP compliant 2-generation reproduction toxicity study conducted according to the EPA OPP 83-4 (as described above), Sprague-Dawley rats (25/sex/group (F0 generation), 30/sex/group (F1 generation)) received triclosan by daily gavage at doses of 0, 300, 1000, and 3000 ppm. Males and females were exposed 10 weeks before mating, during mating, during pregnancy and during lactation until sacrifice. A NOAEL of 1000 ppm was established for neonatal and developmental toxicity based on decreased survival of F1 pups and suggested for F2 pups, and decreased F1 pup body weight during lactation.

Endocrine Activity (E) Score (H, M or L): M

Triclosan was assigned a score of Moderate for endocrine disruption based on appearance on the SIN and TEDX lists, and effects on thyroid and sex hormones observed in animals. GreenScreen® criteria classify chemicals as a moderate hazard for endocrine activity when they are listed on the SIN/TEDX lists, or there are evidences of endocrine activity in animals (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* ChemSec SIN list – Equivalent concern, including endocrine disruption, SIN list 1.0
  - *Screening:* TEDX – Potential endocrine disruptor
- 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.
- EC 2009
  - In a 4-day gavage study in weanling female Long-Evans rats, triclosan (98.2% purity) was administered at doses of 0, 10, 30, 100, 300 or 1,000 mg/kg/day. A dose dependent decrease in thyroid hormones T4 and T3 were reported. This hypothyroxinemia effect was attributed to induction of hepatic CYP enzymes and subsequent increase in glucuronidation and sulfation of thyroid hormone. To demonstrate that the effects were not related to minor dioxin contaminants in the triclosan sample, liver CYP1A1 activity and other phase I and phase II hepatic enzymes under the regulation of AhR were examined and the result was negative.
  - A 20-day female pubertal assay and a 3-day immature rat uterotrophic assay were conducted in Wistar rats. In the pubertal assay, Tricolosan (99.8% pure) was administered orally (unspecified) to post weaning rats (number unspecified) at doses of up to 300 mg/kg/day (each dose level not specified) during post natal day 22 – 42 (treatment frequency unspecified). Triclosan advanced the age of onset of vaginal opening and increased uterine weight at 150 mg/kg/day, indicative of an estrogenic effect (no description of effects at other doses). In the uterotrophic assay, triclosan was either given alone or co-treated with a positive control ethinylestradiol. Triclosan alone did not affect uterine weight, but when co-treated with ethinylestradiol, a dose-dependent increase was observed which iwas higher than the increase in the positive control group. This may be due to decreased catabolism of steroid hormone. In addition, triclosan induced a dose-dependent decrease in thyroid hormone levels in both assays.

- In a drinking water toxicity study, triclosan (purity 99.6%) was administered to female Wistar rats (12/group) at 0, 1, 10 or 50 mg/kg/day from 8 days before mating to lactation day 21. Offspring also received triclosan after weaning. A dose-related decrease in blood thyroid hormone level was observed (T4 and T3). Live birth index and 6-day survival index were significantly reduced at the high dose. There was a decrease of sex ratio (less males) in all dosed groups. The mean body weight of female pups before weaning were lower in all groups, but this effect was not dose-dependent. Female pups treated with triclosan had delayed sexual development exemplified by day of vaginal opening and day of rist estrus, and these animals had a higher body weight at these points in time. The observations in this study are consistent with effects related to thyroid hormone homeostasis disruption and possibly an effect on the hypothalamic-pituitary-ovarian axis.
- SCCP concluded that triclosan can affect thyroid hormone homeostasis in the rat, which is a sensitive model for thyroid hormone changes compared to humans.

An exhaustive literature search was not conducted as available data are sufficient to classify triclosan to Moderate hazard.

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): vH

Triclosan was assigned a score of High for acute toxicity based on an inhalation LC_{50} value being less than 0.5 mg/L for Triclosan. GreenScreen® criteria classify chemicals as a Very High hazard for acute toxicity when an inhalation LC_{50} is equal to or less than 0.5 mg/L for - Dust/Mist/Fume (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* GHS New Zealand – 6.1E (Oral): Acutely toxic (GHS Category 5)
- Oral -
  - ECHA 2014b
    - LD_{50} > 5,000 mg/kg (rats)
- Dermal -
  - ECHA 2014b
    - LD_{50} > 6000 mg/kg (rabbits)
- Inhalation-
  - ECHA 2014b (This study was determined to be not reliable by ECHA because triclosan was dissolved into ethanol for aerosolization, which is not relevant to human exposure scenarios)
    - LC_{50} (4 hr) of 0.286 mg/kg (male rat) and of 0.603 mg/L (female rat)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)
***Group II Score (single dose)*(vH, H, M or L): vH**
Triclosan was assigned a score of Very High for systemic toxicity (single dose) based on systemic toxicity observed at 0.513 mg/L in rats via inhalation and 1,000 mg/kg/day via dermal application in rabbits. GreenScreen® criteria classify chemicals as a Very High hazard for systemic toxicity (single dose) when dermal effect levels are ≤1,000 mg/kg and inhalation effect levels are ≤1.0 mg/L/4h (CPA 2012a).
Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- ECHA 2014b
    - No adverse effects other than emesis and diarrhoea were reported in an acute oral toxicity study in rats at the oral dose of 5000 mg/kg of triclosan.
    - In an acute inhalation toxicity study, Sprague-Dawley rats (10/sex/dose) were exposed nose-only to aerosolized triclosan dissolved in ethanol at concentrations of 0.124, 0.466, 0.513 and 0.678 mg/L for 4 hours. Dyspnea, exophthalmos, and cyanosis were observed (dose not specified). Epistaxis (nosebleed) and chromodacryorrhea (bloody tear) were noted at 0.513 and 0.678 mg/L. Treated animals had reduced body weight gain (dose unspecified) and weight loss at day 7 in both sexes at 0.513 mg/L. It should be noted that this study was considered not reliable by ECHA as inhalation to aerosolized triclosan dissolved in ethanol is not relevant to human exposure scenarios. Nevertheless, ToxServices used this study in the evaluation of this endpoint according to GreenScreen® criteria.
    - In an acute dermal toxicity study, triclosan was applied to the skin of New Zealand rabbits at 1,000 or 6,000 mg/kg. Clinical observations included dyspnea and exophthalmos (bulging of the eye out of the orbit) at both doses. Partially congested organs (unspecified) were found upon necropsy (dose unspecified, probably both). Triclosan induced sings of minimal to slight irritation at 1,000 mg/kg/day at minimal to moderate irritation at 6,000 mg/kg/day that were not reversible. There was no report on whether other effects were reversible. ToxServices determined that systemic toxicity was observed at the dose of 1,000 mg/kg/day based on probable congested organs.

***Group II* Score (repeated dose)*(H, M, or L): M**
Triclosan was assigned a score of Moderate for systemic toxicity (repeated dose) based on animal data. GreenScreen® criteria classify chemicals as a Moderate hazard for systemic toxicity (repeated dose) when animal studies identify oral LOAEL values between 10-100 mg/kg/day, dermal LOAEL values between 20-200 mg/kg/day and inhalation LOAEL values between 0.2-1.0 mg/L (the guidance values are adjusted based on study duration) (CPA 2012a).
- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- Oral –
    - ECHA 2014b
        - The repeated oral dose toxicity of triclosan has been investigated in several animal studies. In a 13-week oral study in mice, a LOAEL of 25 mg/kg/day was identified based on effects on haematology parameters,

relative liver weights and total cholesterol. No NOAEL was identified. The relevance of this study is limited by particular sensitivity in the mouse to peroxisome proliferation, an effect not regarded as relevant to humans. Consequently, a NOAEL of 40 mg/kg/day (male) and 56 mg/kg bw day (female) was identified from a two-year carcinogenicity study in the rat based on clinical chemistry changes, together with histopathological changes in the liver in males and a trend for reduced body weight gain in females. Studies in other species including mice, hamster and baboon also suggest the liver as a target organ.

- Dermal
  - ECHA 2014b
    - Local irritant effects have been clearly seen in animal studies. A NOAEL of 7.5 and 3.5 mg/kg/day was identified in 14-day studies in male and female rats, respectively. No systemic toxicity was seen in the rat studies and the only available robust dog study. However, histological changes to the liver were seen in two 14-day studies in the mouse, with a NOAEL of 20 and 24 mg/kg/day identified in males and females respectively.
    - In a 90 day repeat dose dermal toxicity study in rats (OECD TG No. 411), triclosan was administered in propylene glycol as an occlusive topical application to 10 rats per sex per group at doses of 0, 10, 40 or 80 mg/kg/day for at least 6 hours per day. The only treatment related effect observed was erythema and/or oedema at 10 mg/kg/day and above, with severity increasing with dose. No mortality or clinical signs of toxicity were seen. At necropsy, hyperplasia, hyperkerotosis, inflammation and focal necrosis were seen at the application site. With the exception of one animal, dermal findings were observed to return to normal in the recovery group. As there were no significant clinical chemistry or haematological or histopathological changes to indicate reliable evidence of systemic toxicity, the NOAEL for repeated dose dermal toxicity was considered to be 80 mg/kg/day, the highest dose tested. For local irritant effects, no NOAEL could be identified.
- Inhalation
  - ECHA 2014b
    - In 21-day inhalation study, Sprague-Dawley rats (9/sex/dose) were exposed nose only (5 days/week for 2 h/day) to 10% ethanol aerosol containing tricolsan at doses of 0.05, 0.227 and 1.3 mg/L air. More than 50% of the rats died after the initial single 2-h exposure to 1.3 mg triclosan/L air and therefore the test concentrations were then changed from the second day of treatment to 0.05, 0.115 and 0.301 mg/L air until test ending. Twelve high-dose animals (five males and seven females) died during the course of the study. A NOAEC was established at 0.115 mg/L based on treatment-related effects, including decreased food consumption, reduced body weight gain, slight tendency to leucocytosis probably associated with the slight inflammatory changes seen in the nasal cavity or in the trachea, and increased alkaline phosphatase activity in males only. The experimental design of this study however was considered not appropriate to assess human health hazard of triclosan from repeated inhalation exposures because triclosan exposure would not

be to an aerosol of solubilized, respirable sized triclosan. As a powdered, solid substance triclosan would at worst be a dust but also due to low vapor pressure would give only limited amounts of volitilized material into the atmosphere. Further, the reduction of day 1 exposures and subsequent administration to the same animals increases the uncertainty of the effective exposure concentration inducing the observed effects. Nevertheless this study was considered under GreenScreen® criteria, as GreenScreen® is a hazard-based assessment. The NOAEC of 0.115 and the LOAEC of 0.301 mg/L are converted to 0.082 and 0.215 mg/L after adjustment for treatment frequency (i.e. 5 days/week to 7 days/week). According to GHS classification criteria, the guidance values are multiplied by a factor of 4.3 (13/3) from a 13-week study to a 3-week study. Therefore, the guidance values are 0.086 mg/L (0.02 x 4.3) and 0.86 mg/L for a 21-day study. Therefore, the LOAEC of 0.215 mg/L falls under GHS category 2.

Neurotoxicity (N)

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

Triclosan was assigned a score of data gap for neurotoxicity (single dose) based on a lack of data for this endpoint.

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- Not listed as a potential neurotoxicant on the Red List of Chemicals (CPA 2011d).
- ECHA 2014b
  - In the acute oral toxicity study in rats, animals treated with 5,000 mg/kg triclosan showed hunched posture and lethargy which were reversible by day 7.
  - In the acute inhalation toxicity study in rats, animals showed ruffled fur and curved body position during the exposure period (dose not specified). It was not clear if these effects were reversible after exposure.
  - In the acute dermal toxicity study in rabbits, the treated animals had sedation, ruffled fur, and curved body position at 1,000 and 6,000 mg/kg. Animals in the high dose group also had ataxia.

Available data cited above are not sufficient to classify triclosan under GHS criteria.

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

Triclosan was assigned a score of Moderate for neurotoxicity (repeated dose) based on classification into GHS category 2. GreenScreen® criteria classify chemicals as a Moderate hazard for neurotoxicity (repeated dose) when they are classified to GHS category 2 for repeated exposure (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- Not classified as a developmental neurotoxicant (Grandjean and Landrigan 2006).
- Not listed as a potential neurotoxicant on the Red List of Chemicals (CPA 2011d).
- ECHA 2014b

    - In a 14-day neurotoxicity study, albino rats were exposed orally to triclosan at a dose level of 0, 100, 300, 1000 or 2000 mg/kg/day. A slight inhibition of movement, decreased muscular tone, polydipsia (excessive thirst) and polyuria (increased urination) were observed at 300 mg/kg/day, with more pronounced signs at 1000 mg/kg/day. No changes in brain weights or histopathology and no changes in peripheral nerves were observed at any dose level tested. The NOEL was considered to be 100 mg/kg/day and the LOEL was 300 mg/kg/day.
- The GHS guidance values of 10 and 100 mg/kg/day for 90-day studies are multiplied by a factor of 6.5 (13/2) to 65 and 650 mg/kg/day for 2-week studies. Therefore, the LOEL of 300 mg/kg/day is below the cutoff value for GHS category 2 chemicals.

Skin Sensitization (SnS) Group II* Score (H, M or L): L
Triclosan was assigned a score of Low for skin sensitization based on negative data. GreenScreen® criteria classify chemicals as a low hazard for skin sensitization when adequate negative data are available, there are no structural alerts, and they are not GHS-classified (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- ECHA 2014b
    - In a non-GLP compliant Maurer optimisation test in Pirbright-Hartley guinea pigs, the incidence of positive reactions was similar for triclosan-treated (4/20 after first challenge, 3/20 after second challenge) and negative control animals (4/19 after first challenge, 1/19 after second challenge). The authors concluded that triclosan did not show skin-sensitizing potential in this study.
    - In a GLP compliant Buehler skin sensitization test (EPA OPP 81-6) in Hartley albino guinea pigs, very faint erythema was noted at 6 test sites and all positive control sites exhibited signs of a sensitization response at 24hrs after challenge. It was concluded that contact sensitization did not occur with triclosan.
    - The skin sensitization potential of triclosan was also evaluated in the guinea pig Split adjuvant test. Bright pink and moderately elevated reaction was seen in 1 of 20 animals at 24 and 48 hours post-challenge. At 72 hours, erythema was still present but without oedema. There were no reactions in any of the control group animals. The authors concluded that triclosan has a very low sensitization index.

- Based on weight of evidence, triclosan showed no skin sensitization potential in studies conducted in guinea-pigs.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): DG
Triclosan was assigned a data gap for respiratory sensitization based on a lack of data for this endpoint.

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- No data were identified

Skin Irritation/Corrosivity (IrS) Group II Score (vH, H, M or L): H
Triclosan was assigned a score of High for skin irritation/corrosivity based on being classified as a GHS category 2 Skin Irritant and association with EU R38 and H315. GreenScreen® criteria classify chemicals as a High hazard for skin irritation/corrosivity when adequate data are available, they are associated with EU R38 or H315, or they are GHS category 2-classified (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* EC R38 – Irritating to skin
  - *Authoritative:* EC H315 – Causes skin irritation
  - *Screening:* GHS New Zealand – 6.3A: Irritating to the skin (GHS category 2)
- ECHA 2014b
  - In a non-GLP dermal irritation test similar to draiz test conducted according to the US FDA guidelines, triclosan was applied to the shaved, abraded and non-abraded skin of six rabbits under occlusive conditions for 24 hours. The average score of the 24 and 48-h observations for animals ranged from 1 to 3 for erythema and from 0.5 to 2.0 for edema. Non reversibility of findings after 2 days was observed in some cases. Following GHS criteria a chemical with a score between 2.3 and 4.0 for erythema/eschar or for oedema is classified as a Category 2 Irritant (UN 2013).

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): H
Triclosan was assigned a score of High for eye irritation/corrosivity based on its association with EC H319. GreenScreen® criteria classify chemicals as a High hazard for eye irritation/corrosivity when they are associated with EC H319 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* R36 – Irritating to eyes
  - *Authoritative:* H319 – Causes serious eye irritation
  - *Screening:* GHS New Zealand – 6.4A: Irritating to the eye (GHS category 2A/B)
- ECHA 2014b
  - A non-GLP compliant acute eye irritation/corrosion study (EPA OPP 81-4) was conducted using New Zealand White rabbits (n=6). 0.1 g of triclosan was instilled into the rabbit eye. Triclosan produced irritation characterized by corneal and iridial involvement and conjunctival irritation. The average score of the 24, 48, and 72-h observations for animals ranged from 0.66 to 2.33 for conjunctival redness, from 0.66 to 2.33 for chemosis, from 0.33 to 1 for corneal opacity and from 0 to 1 for iritis. Non reversibility of findings after 7 days was observed in some cases. Following GHS criteria, a score of above 2 for conjunctival redness, and above 2 for chemosis classifies this chemical as a Category 2B eye irritant GHS (UN 2013).

Ecotoxicity (Ecotox)

Acute Aquatic Toxicity (AA) Score (vH, H, M or L): vH
Triclosan was assigned a score of Very High for acute aquatic toxicity based on L/EC50 values being < 1 mg/L and on its association with EU H400 and R50. GreenScreen® criteria classify chemicals as a Very High hazard for acute aquatic toxicity when acute aquatic toxicity values are below 1 mg/L or they are listed with H400/R50 (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Classified in ECHA REACH registration dossier as Aquatic Acute 1 with hazard statement H400: Very toxic to aquatic life.
    - *Authoritative:* EC R50 – Very toxic to aquatic organisms
    - *Screening:* Environment Canada DSL – Inherently toxic in the environment (iT)
    - *Screening:* GHS New Zealand – 9.1A (algal, crustacean, fish) – Very ecotoxic in the aquatic environment (GHS category 1)
- ECHA 2014b
    - An LC_{50} value of 0.54 to 4.37 mg/L was identified for Zebra fish (96-hr).
    - An LC_{50} value of 0.26 mg/L was identified for *Pimephales promelas* (fish, 96-hr).
    - An EC_{50} value of 0.0697 to 0.81 mg/L was identified for *Daphnia magna* (invertebrate, 48-hr).
    - An EC_{25} value (growth) of 10.7 µg/L was identified for *Navicula pelliculosa* (algae, 96 h).
    - An EC_{50} value of 0.78 mg/L was identified for *Scenedesmus subspicatus* (algae, 72h)
    - An EC_{25} value (growth) of 66 µg/L was identified for *Skeletonema costatum* (algae, 96 h)

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): vH

Triclosan was assigned a score of Very High for chronic aquatic toxicity based on chronic toxicity values being below 0.1 mg/L. GreenScreen® criteria classify chemicals as a Very High hazard for chronic aquatic toxicity when chronic aquatic toxicity values are < 0.1 mg/L (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* EC H410 – Very toxic to aquatic life with long lasting effects.
    - *Authoritative:* EC R53 – May cause long-term adverse effects in the aquatic environment
    - *Screening:* Environment Canada DSL – Inherently toxic in the environment
- ECHA 2014b
    - An NOEC value (reproduction) of 6 µg/L was identified for *Ceriodaphnia dubia* (invertebrate, 7-day).
    - An NOEC value (reproduction rate) of 26 µg/L was identified for *Daphnia magna* (invertebrate, 21-day).
    - An NOEC value (mortality) of 34.1 µg/L was identified for *Oncorhynchus mykiss* (fish, 96-day).
    - An NOEC value (fecundity, fertility) ≥ 13.5 µg/L was identified for *Pimephales promelas* (fish, 21-day).
    - An EC_{25} value (growth) of 10.7 µg/L was identified for *Navicula pelliculosa* (algae, 96 h).
    - An EC_{50} value of 0.78 mg/L was identified for *Scenedesmus subspicatus* (algae, 72h)
    - An EC_{25} value (growth) of 66 µg/L was identified for *Skeletonema costatum* (algae, 96 h)

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): H

Triclosan was assigned a score of High for persistence based on weight of evidence and on its classification in a Screening list. GreenScreen® criteria classify chemicals as a High hazard for persistence when available data indicate the chemical is persistence in the soil and is not readily biodegradable (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Environment Canada-Domestic substances list (DSL): Persistent
- ECHA 2014b
  - Based upon results from tests using the standard method OECD 301B (CO2 Evolution, Modified Sturm Test) and 301F (manometric respirometry test), the degradation of triclosan over 28 days was 37%, at 10 mg/L, 18% at 20 mg/L and 52% at 10 µg/L, respectively. Based on these findings, triclosan is not considered readily biodegradable. However, these and other studies with activated sludge under aerobic conditions suggest that triclosan may be inherently biodegradable, with substantial mineralisation to CO2 occurring**.**
  - The biological degradation of triclosan in soil was examined in a study conducted according to the OECD Guideline 307 (Aerobic and Anaerobic Transformation in Soil). The results from his study indicated that aerobic degradation of triclosan in soil proceeds primarily via formation of methyl-triclosan and significant amounts of bound residues. The half-lives of methyl-triclosan at 20 °C were calculated to range from 39 to 153 days depending on the soil type.
  - In another GLP compliant aerobic soil metabolism study conducted at 22 °C, the half-lives of triclosan were calculated to range from 17 to 35 days depending on the soil type. However, triclosan persisted under anaerobic conditions over the 70 day experimental period.

Based on weight of evidence, under anaerobic conditions triclosan is not readily biodegradable and is considered persistent in soil and sediment.

Bioaccumulation (B) Score (vH, H, M, L, or vL): H

Triclosan was assigned a score of High for bioaccumulation based on measured BCF values of 2,532-4,157 in fish and the log K_{ow} of 4.8. GreenScreen® criteria classify chemicals as a High hazard for bioaccumulation when data indicate a BCF between 1000-5000 or the log K_{ow} is between 4.5 and 5 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- ECHA 2014b
  - Log K_{ow} = 4.8
  - In a GLP compliant bioaccumulation study conducted according to the OECD 305C guideline (Bioaccumulation: Test for the Degree of Bioconcentration in Fish), the BCF values of triclosan in zebra fish exposed for 5 weeks to 3 and 30 µg/L at pH 8 were 4157 and 2532, respectively. According to GHS classification criteria, these BCFs suggest bioconcentration in aquatic organisms (Ciba-Geigy 1991).

    - In another non-GLP compliant bioaccumulation study conducted according to the OECD 305E guideline (Bioaccumulation: Flow-through Fish Test), the observed BCF values of triclosan in zebra fish ranged from 3740 (pH 9) and 7900 (pH 6). According to GHS classification criteria, these BCFs suggest bioconcentration in aquatic organisms (Schettgen 2000).
    - In a non-GLP ADME study in goldfish, BCF calculated from measured tissue concentrations of triclosan ranged from 28 to 3,400 at 0.5 – 8 hours. The data were not lipid normalized due to lack of data on lipid content.
    - The two bioaccumulation studies described above (i.e. Ciba study and Schettgen study) were evaluated and their limitations were discussed in a review article. It was concluded that there is a higher level of uncertainty in the BCF reported by the Schettgen study due to limitations in test media preparation, high variation in the recovery of triclosan in the fish tissue and high concentrations of methanol used.
    - In a GLP-compliant terrestrial bioaccumulation study in earthworm (*Eisenia fetida*) performed according to OECD TG317, BCF values were 0.59 – 52.1.
- EC 2009
    - Based on tissue distribution and plasma AUC data in hamsters and rats, respectively, triclosan is concluded to lack bioaccumulation/bioretention. Tissue distribution data in mice indicated increased triclosan levels in the liver compared to plasma.

Based on the data above, triclosan is bioaccumulative in the aquatic environment. Although the Schettgen study reported a BCF of > 5,000 that would have classified triclosan to Very High under GreenScreen® criteria, a later review article indicated that this study was not reliable as the GLP-compliant Ciba study, which reported a BCF of between 1,000 and 5,000, which is also consistent with results obtained from a third bioaccumulation study. Therefore, ToxServices used these lower BCF values to classify triclosan for this endpoint. On the other hand, toxicokinetics studies in mammalian species suggest that this compound is not accumulated in tissues.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): L

Triclosan was assigned a score of Low for reactivity based on not having any chemicals or functional groups expected to contain high energy bonds or oxidizing species which may cause reactivity. This chemical would not be classified for reactivity under GHS (UN 2013). GreenScreen® criteria classify chemicals as a Low hazard for reactivity when it is not explosive, unless there are data showing otherwise (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* not listed in any authoritative lists
    - *Screening:* not listed in any screening lists
- ECHA 2014b
    - Triclosan would not be classified as an oxidizing chemical as it does not contain structural groups that would cause concern for explosion.

Flammability (F) Score (vH, H, M or L): L

Triclosan was assigned a score of Low for flammability based on experimental data. GreenScreen® criteria classify chemicals as a low hazard for flammability when adequate data available and GHS not Classified (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* not listed in any authoritative lists
    - *Screening:* not listed in any screening lists
- ECHA 2014b
    - In a GLP compliant flammability test conducted according to EEC Directive 92/69 guideline (Method A.10 (Flammability (Solids)), tricolsan was determined to be not flammable**.**

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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

(Cr) Corrosion/ Irritation (Skin/ Eye)

(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 Triclosan (CAS #3380-34-5)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

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**
No	Triclosan	3380-34-5	**L**	**L**	**M**	**M**	**M**	**vH**	**vH**	**M**	DG	*M*	**L**	DG	**H**	**H**	**vH**	**vH**	**H**	**H**	**L**	**L**

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen™ Benchmark Score
Triclosan	1

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

Table 6

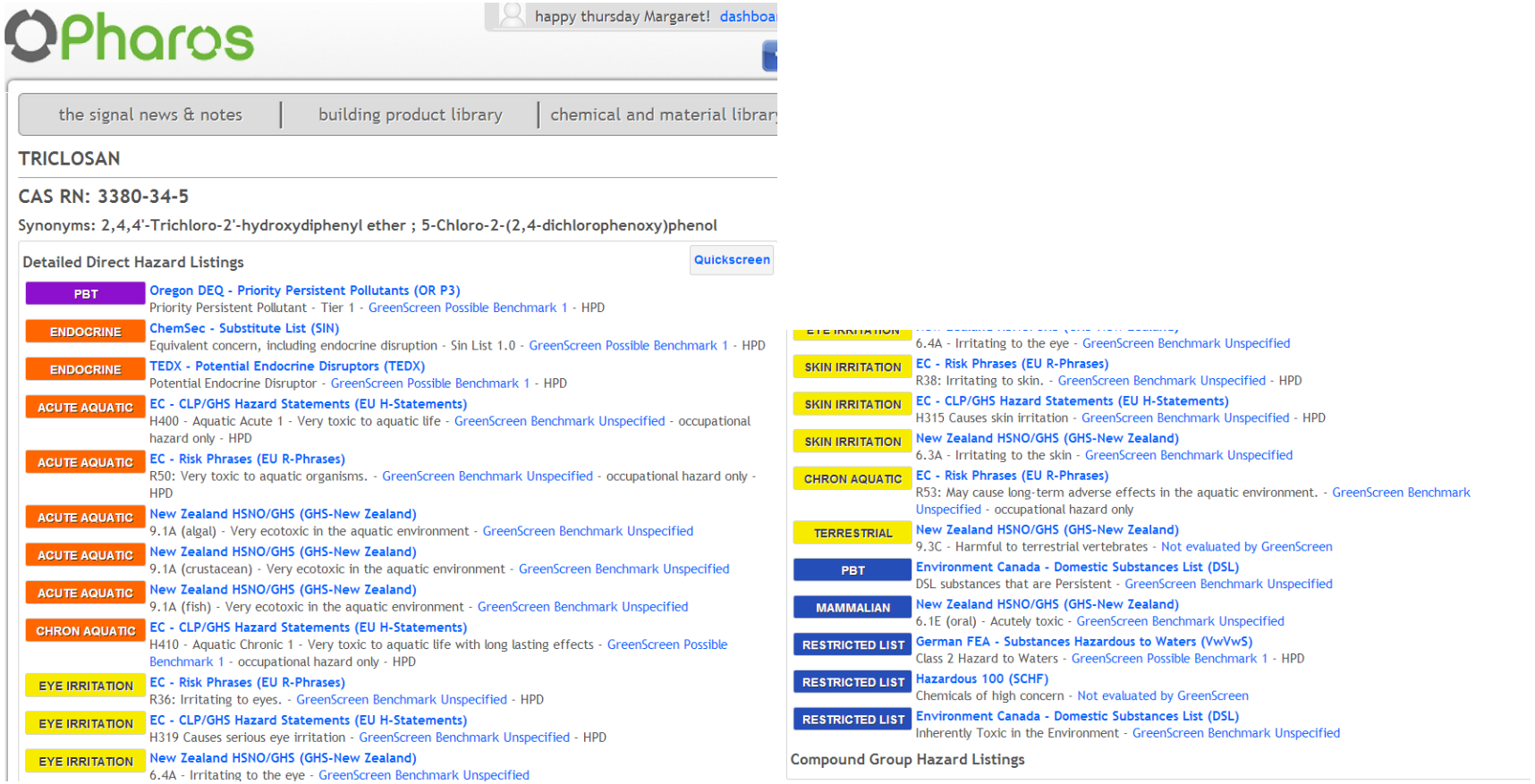
Chemical Name	Final GreenScreen™ Benchmark Score
Triclosan	1

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 Triclosan (CAS #3380-34-5)



Pharos

happy thursday Margaret! dashboa

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TRICLOSAN

CAS RN: 3380-34-5

Synonyms: 2,4,4'-Trichloro-2'-hydroxydiphenyl ether ; 5-Chloro-2-(2,4-dichlorophenoxy)phenol

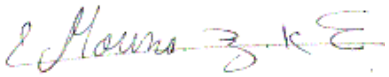
Detailed Direct Hazard Listings — Quickscreen

PBT	Oregon DEQ - Priority Persistent Pollutants (OR P3) Priority Persistent Pollutant - Tier 1 - GreenScreen Possible Benchmark 1 - HPD
ENDOCRINE	ChemSec - Substitute List (SIN) Equivalent concern, including endocrine disruption - Sin List 1.0 - GreenScreen Possible Benchmark 1 - HPD
ENDOCRINE	TEDX - Potential Endocrine Disruptors (TEDX) Potential Endocrine Disruptor - GreenScreen Possible Benchmark 1 - HPD
ACUTE AQUATIC	EC - CLP/GHS Hazard Statements (EU H-Statements) H400 - Aquatic Acute 1 - Very toxic to aquatic life - GreenScreen Benchmark Unspecified - occupational hazard only - HPD
ACUTE AQUATIC	EC - Risk Phrases (EU R-Phrases) R50: Very toxic to aquatic organisms. - GreenScreen Benchmark Unspecified - 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
ACUTE AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1A (crustacean) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified
ACUTE AQUATIC	New Zealand HSNO/GHS (GHS-New Zealand) 9.1A (fish) - Very ecotoxic in the aquatic environment - GreenScreen Benchmark Unspecified
CHRON AQUATIC	EC - CLP/GHS Hazard Statements (EU H-Statements) H410 - Aquatic Chronic 1 - Very toxic to aquatic life with long lasting effects - GreenScreen Possible Benchmark 1 - occupational hazard only - HPD
EYE IRRITATION	EC - Risk Phrases (EU R-Phrases) R36: Irritating to eyes. - GreenScreen Benchmark Unspecified - HPD
EYE IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements) H319 Causes serious eye irritation - GreenScreen Benchmark Unspecified - HPD
EYE IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.4A - Irritating to the eye - GreenScreen Benchmark Unspecified
SKIN IRRITATION	EC - Risk Phrases (EU R-Phrases) R38: Irritating to skin. - GreenScreen Benchmark Unspecified - HPD
SKIN IRRITATION	EC - CLP/GHS Hazard Statements (EU H-Statements) H315 Causes skin irritation - GreenScreen Benchmark Unspecified - HPD
SKIN IRRITATION	New Zealand HSNO/GHS (GHS-New Zealand) 6.3A - Irritating to the skin - GreenScreen Benchmark Unspecified
CHRON AQUATIC	EC - Risk Phrases (EU R-Phrases) R53: May cause long-term adverse effects in the aquatic environment. - GreenScreen Benchmark Unspecified - occupational hazard only
TERRESTRIAL	New Zealand HSNO/GHS (GHS-New Zealand) 9.3C - Harmful to terrestrial vertebrates - Not evaluated by GreenScreen
PBT	Environment Canada - Domestic Substances List (DSL) DSL substances that are Persistent - GreenScreen Benchmark Unspecified
MAMMALIAN	New Zealand HSNO/GHS (GHS-New Zealand) 6.1E (oral) - Acutely toxic - GreenScreen Benchmark Unspecified
RESTRICTED LIST	German FEA - Substances Hazardous to Waters (VwVwS) Class 2 Hazard to Waters - GreenScreen Possible Benchmark 1 - HPD
RESTRICTED LIST	Hazardous 100 (SCHF) Chemicals of high concern - Not evaluated by GreenScreen
RESTRICTED LIST	Environment Canada - Domestic Substances List (DSL) Inherently Toxic in the Environment - GreenScreen Benchmark Unspecified

Compound Group Hazard Listings

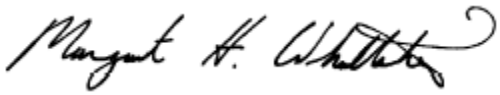
Authorized Reviewers

Triclosan GreenScreen® Evaluation Prepared By:



Mouna Zachary, PhD
Toxicologist
ToxServices LLC

Triclosan GreenScreen® Evaluation QC'd By:



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