Triclocarban (CAS# 101-20-2) GreenScreen® for Safer Chemicals (GreenScreen®) Assessment

Prepared by:

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GreenScreen® Executive Summary for Triclocarban (CAS #101-20-2)

Triclocarban (TCC) or 3,4,4'-trichlorocarbanilide, is a substance with anti-bacterial and anti-fungal properties that is used globally in a wide range of personal cleansing products.

Triclocarban was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") due to high persistence (P), moderate Group I human Toxicity due to moderate reproductive toxicity (R) and endocrine activity (E), moderate Group II Human Toxicity due to moderate skin and eye irritation potentials (IrS and IrE), moderate Group II* Human due to moderate repeated dose systemic toxicity (STr), and very high Ecotoxicity due to very high acute and chronic aquatic toxicity (AA and CA). This corresponds to GreenScreen® benchmark classifications 2c, 2e and 2f in CPA 2011. Data gaps (DG) exist for neurotoxicity (single and repeated N) 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), triclocarban meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if triclocarban were assigned a Very High score for the data gap Nr and SnR, or a High score for Ns, it would still be categorized as a Benchmark 2 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 2 ("Use but Search for Safer Substitutes") assigned to triclocarban is applicable for all routes of exposure.

GreenScreen® Hazard Ratings for Triclocarban

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**	**L**	**M**	**L**	**L**	**M**	DG	DG	**L**	DG	**M**	**M**	**vH**	**vH**	**H**	**L**	**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 Triclocarban (CAS #101-20-2)

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

Chemical Name: Triclocarban

CAS Number: 101-20-2

GreenScreen® Assessment Prepared By:
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Date: January 20, 2014, May 27, 2014

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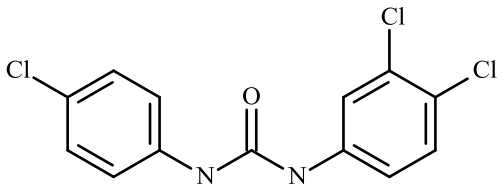
Title: Managing Director and Chief Toxicologist
Organization: ToxServices LLC
Date: February 7, 2014; May 27, 2014

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

Chemical Structure(s):



Triclocarban (CAS#101-20-2)

Also called: 3,4,4'-Trichlorocarbanilide; N-(4-Chlorophenyl)-N'-(3,4-dichlorophenyl)urea; TCC;1-(3',4'-Dichlorophenyl)-3-(4'-chlorophenyl)urea; Carbanilide, 3,4,4'-trichloro-; Cusiter; Cutisan; Genoface (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 (ChemIDplus 2014)
2. Bacteriostat (ChemIDplus 2014)
3. Germicide (ChemIDplus 2014).

Triclocarban is a limited spectrum antimicrobial, and targets certain bacteria and fungi by inhibiting the activity of the enzyme enoyl-acyl carrier protein reductase, which helps build cell membranes in bacteria and fungi. The European Union specifies that triclocarban may

[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

be used as a preservative up to 0.2%, but it may be used at higher levels for other purposes. The EU SCCP concluded that a maximum concentration of 1.5% in cosmetic rinse-off hand and body care products was unlikely to pose a direct human health risk (SCCP 2005). In North America, TCC is used exclusively as an antimicrobial and preservative in bar and liquid soaps and body washes (SDA 2002a).

GreenScreen® Summary Rating for Triclocarban [2]: Triclocarban was assigned a GreenScreen® Benchmark Score of 2 ("Use but Search for Safer Substitutes") due to high persistence (P), moderate Group I human Toxicity due to moderate reproductive toxicity (R) and endocrine activity (E), moderate Group II Human Toxicity due to moderate skin and eye irritation potentials (IrS and IrE), moderate Group II* Human due to moderate repeated dose systemic toxicity (STr), and very high Ecotoxicity due to very high acute and chronic aquatic toxicity (AA and CA). This corresponds to GreenScreen® benchmark classification 2c, 2e and 2f in CPA 2011. Data gaps (DG) exist for neurotoxicity (single and repeated N) 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), triclocarban meets requirements for a GreenScreen® Benchmark Score of 2 despite the hazard data gaps. In a worst-case scenario, if triclocarban were assigned a Very High score for the data gap Nr and SnR, or a High score for Ns, it would still be categorized as a Benchmark 2 Chemical.

Figure 1: GreenScreen® Hazard Ratings for Triclocarban

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	L	M	L	L	M	DG	DG	L	DG	M	M	vH	vH	H	L	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]

No environmental transformation products were identified for triclocarban. It is not expected to undergo hydrolysis or direct photolysis as it lacks functional groups susceptible to these reactions (HSDB 2012). Triclocarbon is expected to be immobile in soil and its volatilization

[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.

from water is considered low based on its estimated Henry's Law constant[4] of 4.5 x 10^{-11} atm m^3/mol at 25ºC.

Introduction

Triclocarban (TCC) or 3,4,4'-trichlorocarbanilide, is a substance with anti-bacterial and anti-fungal properties that is used globally in a wide range of personal cleansing products (ChemIDplus 2014). Triclocarban has been marketed for more than 45 years around the world, and is used in bar and liquid soaps, detergents, body washes and wipes (SDA 2002a). Triclocarban is allowed for use as a preservative at levels up to 0.2% in cosmetic products in the European Union. However, it can be used at higher concentrations in cosmetics for use as a non-preservative (provided data to substantiate its safety are submitted to SCCP) and a safe level of 1.5% was approved for cosmetic rinse-off hand and body care products by the EU (SCCP 2005). Based on the results of a Soap and Detergent Association Use and Exposure Survey (SDA 2002b), bar soaps contain levels of triclocarban which range from 0.5 to 5% in the final formulation, liquid soaps contain triclocarban at levels ranging from 1 to 5% and body washes may contain from 0.1 – 0.5% in the final formulation. ToxServices assessed triclocarban 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 (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 triclocarban can be found in Appendix C and a summary of the results can be found below:

- High hazard of PBT: EC/Oslo-Paris Conv-Priority PBTs and EDs and equivalent concern (OSPAR): PBT-Substance of possible concern
- Medium hazard of Endocrine: TEDX- Potential Endocrine Disruptors (TEDX): Potential Endocrine Disruptor
- Potential concern: Restricted List- Environment Canada-Domestic Substance List (DSL): Inherently Toxic in the Environment; DSL substances that are persistent

PhysioChemical Properties of Triclocarban

The physiochemical properties of Triclocarban are summarized in Table 1. Triclocarban is a white, odorless powder with experimental log K_{ow} value greater than 4 indicating its potential to bioaccumulate is high. It is slightly soluble in water and is lighter than water. Triclocarban has a low vapour pressure, suggesting low volatility.

[4] Henry's Law states that the solubility of a gas in a liquid is directly proportional to the partial pressure of the gas above the liquid: $C = kP_{gas}$, where C is the solubility of a gas at a fixed temperature, k is the Henry's law constant and P_{gas} is the partial pressure of the gas. A Henry's law constant (atm-m^3/mole) of less than 10^{-7} indicates that a compound is nonvolatile (U.S. EPA 2013)

Table 1: Physical and Chemical Properties of Triclocarban (CAS #101-20-2)		
Property	**Value**	**Reference**
Molecular formula	$C_{13}H_9Cl_3N_2O$	ChemIDplus 2014
SMILES Notation	c1cc(ccc1NC(=O)Nc2ccc(c(c2)Cl)Cl)Cl	ChemIDplus 2014
Molecular weight	315.5861	ChemIDplus 2014
Physical state	Powder	ECHA 2014
Appearance	White	ECHA 2014
Melting point	255.2 - 256°C	ECHA 2014
Vapor pressure	< 1 hPa at 50°C 2.73 x 10^{-8} mm Hg at 25ºC (est)	ECHA 2014
Water solubility	0.11 mg/L at 20°C	ECHA 2014
Dissociation constant (pKa)	0.24×10^{-13} at 30°C	ECHA 2014
Density/specific gravity	0.401 g/cm^3 at 35°C	ECHA 2014
Partition coefficient (log K_{OW})	4.2-6	ECHA 2014

Hazard Classification Summary Section:

Group I Human Health Effects (Group I Human)

Carcinogenicity (C) Score (H, M or L): L
Triclocarban 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
  - SCCP 2005
    - In a chronic feeding study, Sprague-Dawley rats (80/sex/dose) received triclocarban at doses of 0, 25, 75 and 250 mg/kg/day for 2 years. Of these groups, clinical evaluations (hematology, clinical chemistry and urinalysis) were carried out at 6, 12, 20, 23 (males) and 25 (females) months. At study termination, all animals were subject to complete necropsy and pathological examination. There was no evidence of a dose-related increase in tumor incidence in any of the treated rats.
    - There was no evidence of carcinogenicity in a chronic toxicity study in which rats were fed with a diet containing doses of triclocarban of 3,000 and 10,000 ppm for 24 months (No further information was provided).

Mutagenicity/Genotoxicity (M) Score (H, M or L): L
Triclocarban was assigned a score of Low for mutagenicity/genotoxicity based on negative results obtained from *in vitro* 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, they

chemical has no structural alerts for genotoxicity and is not classified under GHS (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- SCCP 2005
    - 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 5000 µg/plate, in the presence and absence of metabolic activation. No increase in revertants was observed and triclocarban was reported as negative for mutagenicity under the tested conditions.
    - In another Ames test utilizing *Salmonella typhimurium* tester strains TA98, TA100, TA1535, TA1537 and TA1538, triclocarban was not mutagenic with and without metabolic activation.
    - A GLP-compliant *in vitro* mammalian chromosome aberration test was conducted utilizing Chinese hamster ovary cells at concentrations of up to 2000 µg/mL, in the presence and absence of metabolic activation. Triclocarban was negative for the induction of structural and numerical chromosome aberrations in CHO cells.

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

Triclocarban was assigned a score of Moderate for reproductive toxicity based on reduced pregnancy rate and number of live pups at birth in the second generation in a three-generation rat study, reduced testes weight and small flaccid testes in rats without pathological findings in a 2-year rat study, and effects on live birth index at a very high oral dose in rats. 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.
- SCCP 2005
    - The reproductive and developmental toxicity of triclocarban was evaluated in a three generation oral feeding study. Three successive generations of Sprague-Dawley rats were exposed to triclocarban via the diet at concentrations of 250, 500, 1000 or 3000 ppm (approximately 23, 50, 95 or 280 mg/kg/day). Dosing of F0 rats began 60 days prior to mating and was continuous thereafter. F1and F2 rats were dosed for an 80-day period prior to mating and continuously thereafter. Each parental generation was mated twice, with the first litter sacrificed at weaning and examined for gross abnormalities. Dead or stillborn pups were also examined. No treatment-related effects were observed on mortality, clinical signs of toxicity, body weight, food consumption, mating indices, male fertility or gross malformations in offspring. The pregnancy rate was unusually low at the high dose during the second litter interval of the F1 generation. The mean number of live pups at birth was lower than controls for both litter intervals of the F1 generation receiving the high dose. Based on low pregnancy rate and lower mean number of live pups at birth, the no observed adverse effects level (NOAEL) for reproductive and developmental toxicity were determined to be 3000 ppm (approximately 280 mg/kg/day) for the F0 generation, 1000 ppm (approximately

95 mg/kg/day) for the F1 generation and 3000 ppm (approximately 300 mg/kg/day) for the F2 generation.

- U.S. EPA 2009
    - In the 24-month chronic toxicity in Sprague-Dawley rats as described above, there was a decrease in testes weight and an increase in the incidence of small flaccid testes at the highest dose (i.e. 250 mg/kg/day). However, no abnormal histopathological observations were found.
- ECHA 2014
    - A one-generation reproductive toxicity study in rats was described with limited details, which was taken from the RTECS database. A TDLo was established at 9,000 mg/kg based on effects on live birth index (measured after birth). No other details were available.

Developmental Toxicity incl. Developmental Neurotoxicity (D) Score (H, M or L): L
Triclocarban was assigned a score of Low for developmental toxicity based no evidence of developmental toxicity seen in animal studies. GreenScreen® criteria classify chemicals as a Low hazard for developmental toxicity when adequate data are available and studies are negative for reproductive effects (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- SCCP 2005
    - In the three generation oral feeding study described above, no treatment-related effects were seen on any pups from all generations (including dead pups). Litter viability and survival rates were comparable to controls. The NOAEL for teratogencity was greater than 3000 ppm.

Endocrine Activity (E) Score (H, M or L): M
Triclocarban was assigned a score of Moderate for endocrine disruption based on its classification in screening lists. GreenScreen® criteria classify chemicals initially as a Moderate hazard for endocrine disruption when they are listed in screening lists such as TEDX and OSPAR (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:*
        - High hazard of Endocrine: Listed as a potential endocrine disruptor on the OSPAR List of Chemicals of Possible Concern.
        - Medium hazard of Endocrine-Listed on the TEDX List of Potential Endocrine Disruptors
    - Lasley 2011
        - Triclocarban augments the biological effect of circulating testosterone *in vitro* and changes the morphology of accessory sex organs in male rats, including the prostate gland.

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): L

Triclocarban was assigned a score of Low for acute toxicity based on oral and dermal LD_{50} values being > 2,000 mg/kg for Triclocarban. GreenScreen® criteria classify chemicals as a Low hazard for acute toxicity when dermal and oral LD_{50} values are > 2,000 mg/kg (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- Oral -
  - ECHA 2014
    - LD_{50} > 2,000 mg/kg (rats)
    - LD_{50} > 5,000 mg/kg (mice)
- Dermal -
  - ECHA 2014
    - LD_{50} of 10,000 mg/kg (rabbits)

Systemic Toxicity/Organ Effects incl. Immunotoxicity (ST)

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

Triclocarban was assigned a score of Low for systemic toxicity (single dose) based on no effect levels seen at single oral and dermal doses greater than 2,000 mg/kg, which make triclocarban non-classifiable under GHS. GreenScreen® criteria classify chemicals as a Low hazard for systemic toxicity (single dose) 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.

- Oral
  - SCCP 2005
    - In a GLP compliant oral acute toxicity study (OECD 401), no adverse effects or mortalities were observed in rats administered a single oral dose of 2000 mg/kg triclocarban.
- Dermal
  - SCCP 2005
    - No mortalities or signs of toxicity were observed in New Zealand White rabbits administered unspecified concentrations of triclocarban (0.2 fractional log intervals) to clipped, intact skin under occluded conditions for 24 hours. Duration of the observation period was not indicated.

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

Triclocarban was assigned a score of Moderate for systemic toxicity (repeated dose) based on the lowest LOAEL of 75 mg/kg/day in a chronic dietary study in rats. 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 (CPA 2012a).

- Authoritative and Screening Lists
    - *Authoritative:* Not listed on any authoritative lists.
    - *Screening:* Not listed on any screening lists.
- Oral –
    - ECHA 2014
        - In a GLP complaint 30-day repeat dose oral toxicity study, exposure of Sprague-Dawley rats (10/sex /group) to 25% aqueous solution of triclocarban at 0 (controls), 500 or 1000 mg/kg by intubation 5 days a week resulted in no effects on mortality, body weight or feed consumption. A no observed-adverse-effect level (NOAEL) of 1000 mg/kg was established.
    - SCCP 2005
        - In 8-weeks toxicity study, Sprague-Dawley rats (35/dose) were exposed to triclocarban (purity 98.6%) in the diet at concentrations equivalent to 25, 75 and 250 mg/kg/day. No control group was included in the study. Animals were observed twice daily for morbidity and mortality and once daily for clinical signs. Body weight, food consumption and detailed clinical signs were recorded weekly. Blood samples were taken from 5 animals per group every two weeks for evaluation of blood levels of triclocarban. No necropsy was performed at the end of the study. There were no signs of toxicity or treatment related mortalities throughout the study. Mean bodyweight and food consumption were lower in the highest dose group, however the statistical significance of this difference could not be evaluated due to the absence of a control group. No compound-related pathological or histopathological findings were noted. Based on body weight data, a NOAEL of 75 mg/kg/day was established. However the experimental design of this study was considered not adequate due to the absence of a control group.
        - In a chronic feeding study conducted according to a protocol approved by Food and Drug Administration, Sprague-Dawley rats (80/sex/dose) were administered triclocarban via the diet at 0, 25, 75 or 250 mg/kg/day for 24 months. Interim sacrifices of 10 rats/sex/dose were performed after 6, 12 and 20 months of dosing. No clinical signs of toxicity or treatment-related mortality or changes in food consumption were observed. Mean body weight of males at 250 mg/kg/day and females at 75 and 250 mg/kg/day were slightly reduced compared to controls during most of the study. Anemia was seen in males at 75 and 250 mg/kg/day and in females at 250 mg/kg/day. A slight increase in alkaline phosphatase activity, BUN, glucose and total bilirubin was observed at various time points for in males at high dose. Organ weight changes (specified as increases when discussed in relation to microscopic changes) were seen in the liver (both sexes at 75 and 250 mg/kg/day), spleen (at 75 and 250 mg/kg/day (males); at 250 mg/kg/day (females)), testes and heart weights (at 250 mg/kg/day in males). No microscopic changes were noted in any organs to account for increases in organ weights. Gross pathological changes included an increased incidence of small and flaccid testes in

males at 250 mg/kg/day that died spontaneously or were killed moribund between 12 and 23 months. Based on anemia and increases in organ weights, the NOAEL and LOAEL for the study were considered to be 25 and 75 mg/kg/day respectively.

Neurotoxicity (N)
Group II Score (single dose)**(vH, H, M or L):** DG
Triclocarban 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).
- No data were identified.

Group II* Score (repeated dose)**(H, M, or L):** DG
Triclocarban was assigned a score of data gap for neurotoxicity (repeated 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).
- No data were identified.

Skin Sensitization (SnS) Group II* Score (H, M or L): L
Triclocarban 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.
- SCCP 2005
  - In a GLP skin maximization test conducted according to the Magnusson-Kligman protocol (OECD 406), 2% formulated suspension of triclocarban was found to be non-sensitizing in guinea pigs.
  - The skin sensitization potential of triclocarban was further evaluated in a series of human repeat insult patch tests (HRIPT). Bar soap formulations containing up to 1.5% triclocarban were tested in these studies. No evidence of skin sensitization was seen in these studies.

Respiratory Sensitization (SnR) Group II* Score (H, M or L): DG
Triclocarban 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): M
Triclocarban was assigned a score of Moderate for skin irritation/corrosivity based on none to mild irritation observed in animals and humans. GreenScreen® criteria classify chemicals as a Moderate hazard for skin irritation when they are classified to GHS category 3 (mild irritant) (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists.
- SCCP 2005
  - The skin irritation potential of triclocarban has been evaluated in rabbits and guinea pigs under occluded and non-occluded exposure conditions at concentrations from 0.5% to 100% for 4 and/or 24 hours. Observations were made over a period of several days after the exposure and the exposed skin sites were graded for skin irritation according to the Draize scoring scale. Under fully occluded conditions, neither 24h exposure to a 25% corn oil suspension of triclocarban nor 4h exposure to undiluted triclocarban resulted in any signs of skin irritation in rabbits. Accordingly, triclocarban was classified as non-irritating under the conditions tested.
  - The potential irritant effect of a 10% aqueous solution of a triclocarban-containing bar soap was further investigated in the vaginal tissue of New Zealand rabbits. Under the study conditions chosen, the investigators determined a maximum composite group average score of 6.3 which indicated only a mild irritation of the vaginal tissue of rabbits.
  - The cumulative skin irritation effects of aqueous solutions of triclocarban-containing bar (1.5% triclocarban) and liquid soaps (0.15%) were evaluated under fully occlusive conditions in several human 3-Patch application tests. Under the test conditions chosen, the triclocarban containing products were only slightly irritating to human skin.
  - In a 21-day cumulative patch test, 9% triclocarban in petrolatum applied to human skin elicited only a mild skin irritation response.

Eye Irritation/Corrosivity (IrE) Group II Score (vH, H, M or L): M
Triclocarban was assigned a score of Moderate for eye irritation/corrosivity based on none to slight eye irritation observed in rabbits. GreenScreen® criteria classify chemicals as a Moderate hazard for eye irritation when they are classified to GHS category 2B (mildly irritating) (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* Not listed on any authoritative lists.
  - *Screening:* Not listed on any screening lists
- SCCP 2005
  - A GLP compliant acute eye irritation/corrosion study (OECD 405) was conducted using New Zealand White rabbits. 0.1 ml of triclocarban (purity 98.8%), equivalent to approximately 42 mg was instilled into the rabbit eye. No effects in the cornea, iris, conjunctivae or aqueous humour were observed in any rabbit at any time. Based on this, triclocarban was considered to be not irritating to the rabbit eye.
  - In another study, 20 mg of neat powder from two different samples of triclocarban containing varying levels of impurities (i.e., sample 1 contained 6 -

8% 4,4'-dichlorocarbanilide and 6 - 8% 3,3',4,4'-tetrachlorocarbanilide; sample 2 contained 15 - 20% 4,4'-dichlorocarbanilide and 15 - 20% 3,3',4,4'-tetrachlorocarbanilide) were placed in the conjunctival sac of the right eye of each of three albino rabbits. The eye irritation index calculated according to the method of Draize was 7.3 for the first sample and 6.6 for the second sample, indicating that the test products were only slightly irritating to rabbit eyes.

- The potential irritant effect of a 10% aqueous solution of bar soap containing up to 0.55% triclocarban was further investigated in three GLP studies conducted using New Zealand rabbits. The application of triclocarban in liquid soap and bar soap was virtually non-irritating to the rabbit eye, especially if the eyes were rinsed shortly after application of the product. Symptoms observed were restricted to swelling of the iris as well as redness and discharge from the conjunctivae.

Ecotoxicity (Ecotox)

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

Triclocarban was assigned a score of Very High for acute aquatic toxicity based on L/EC50 values being < 1 mg/L and on its classification on authoritative and screening lists. GreenScreen® criteria classify chemicals as a Very High hazard for acute aquatic toxicity when acute aquatic toxicity values are below 1 mg/L (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* OSPAR: PBT- Substances of possible concern.
  - *Screening:* High hazard of PBT – Environment Canada-Domestic substances list (DSL): Inherently Toxic in the Environment (iT)
- ECHA 2014, ECOTOX 2014
  - The LC_{50} value of 0.140 mg/L was identified for *Ictalurus punctatus* (channel catfish, 96-hr).
  - LC_{50} = 0.04 -0.750 mg/L in *Lepomis macrochirus* (bluegill, 96-hr)
  - LC_{50} = 0.12 mg/L in *Oncorhynchus mykiss* (rainbow trout, 96-hr)
  - LC_{50} = 0.092 mg/L was identified for *Pimephales promelas* (fathead minnow, 96-hr).
  - LC_{50} = 0.0077 – 0.020 mg/L was identified for *Daphnia magna* (invertebrate, 48-hr).
  - An EC_{50} value of 0.003 mg/L was identified for *Ceriodaphnia dubia* (invertebrate, 48-hr).
  - EC_{50} = 0.032 mg/L in *Mercenaria mercenaria* (hard clam, saltwater, 48-hr)
  - LC_{50} = 0.099 mg/L in *Penaeus duorarum* (northern pink shrimp, saltwater, 96-hr)
  - LC_{50} = 0.013 mg/L in *Gammarus fasciatus* (scud, 72-hr)
  - LC_{50} = 0.230 mg/L in *Asellus sp.* (aquatic sowbug, 96-hr)
  - LC_{50} = 0.010 – 0.015 mg/L in *Americamysis bahia* (opossum shrimp, saltwater, 96-hr)
  - LC_{50} = 0.85 mg/L in *Palaemonetes pugio* (daggerblade grass shrimp, saltwater, 96-hr)
  - The LOEC value (growth and biomass) of 0.01-0.05 mg/L was identified for *Pseudokirchneriella subcapitata* (green algae, 72-hr).

Chronic Aquatic Toxicity (CA) Score (vH, H, M or L): vH
Triclocarban 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:* OSPAR: PBT- Substances of possible concern.
  - *Screening:* Environment Canada-Domestic substances list (DSL): Inherently Toxic in the Environment (iT)
- ECHA 2014, ECOTOX 2014
  - The LOEL value (mortality) of 0.01 mg/L was identified for *Pimephales promelas* (fish, 30-day).
  - LOEC = 0.00012 – 0.0006 mg/L in *Americamysis bahia* (opossum shrimp, saltwater invertebrate, 28-day).
  - An LOEC value (survival) of 0.0005 - 0.05 mg/L was identified for *Daphnia magna* (invertebrate, 14-day/21-day).

Environmental Fate (Fate)

Persistence (P) Score (vH, H, M, L, or vL): H
Triclocarban was assigned a score of High for persistence based on being tested as not readily biodegradable but inherently biodegradable with a half-life of 108 days in soil, and on its classification in DSL as persistent. GreenScreen® criteria classify chemicals as a High hazard for persistence when available data indicate the chemical is not readily biodegradable, has a half-life of between 60 and 180 days in soil, and when the chemical is listed in a DSL screening list as persistent (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* OSPAR: PBT- Substances of possible concern.
  - *Screening:* Environment Canada-Domestic Substance List (DSL): substances that are persistent
- HSDB 2012
  - In a ready biodegradability: modified MITI test using activated sludge inoculum, 0% of triclocarban had degraded after 28 days. Triclocarban is not readily biodegradable**.**
  - In other biodegradation studies in continuous flow with activated sludge, triclocarban showed 50-100% degradation in 12 weeks, with lag periods of up to two weeks.
- U.S. EPA 2009
  - No biodegradation under anaerobic conditions in 3 months. Triclocarban is expected to have moderate persistence.
- ECHA 2014
  - Triclocarban was demonstrated to be inherently biodegradable with 98% degradation during wastewater treatment through a combination of sorption and biodegradation processes.
  - In soil, triclocarban was shown to have an aerobic half-life of 108 days.
- Available data above indicated that triclocarban is not readily biodegradable, but inherently degradable, with a half-life of 108 days in soil.

Bioaccumulation (B) Score (vH, H, M, L, or vL): L
Triclocarban was assigned a score of Low for bioaccumulation based on its highest measured BCF of 137 in fish. GreenScreen® criteria classify chemicals as a Low hazard for bioaccumulation when BCFs/BAFs are between 100 and 500 (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* OSPAR: PBT- Substances of possible concern.
  - *Screening:* Not listed on any screening lists.
- ECHA 2014
  - Triclocarban has experimental Log K_{ow} values in the range of 4.2-6.
  - Measured BCF = 80 (20 µg/L) or 81 (2 µg/L) in common carp, indicating no bioaccumulation potential.
- U.S. EPA 2009
  - BCF = 137 in fish (measured in catfish). It was concluded that triclocarban has low potential for bioaccumulation.

Log K_{ow} values measure the inherent tendency of chemicals to partition between aqueous and liquid phases. It can be used to estimate bioaccumulation potential of nonionic organic compounds. However, it does not consider metabolism (UWRL Undated). Therefore, BCF/BAF is a more reliable parameter to evaluate bioaccumulation potential.

Physical Hazards (Physical)

Reactivity (Rx) Score (vH, H, M or L): L
Triclocarban 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 they are not explosive unless there are data stating otherwise (CPA 2012a).

- Authoritative and Screening Lists
  - *Authoritative:* not listed in any authoritative lists
  - *Screening:* not listed in any screening lists
- ECHA 2014
  - Triclocarban would not be classified as an oxidizing chemical as it does not contain structural groups that would cause concern for explosion.
- Shiva Pharmachem Undated
  - Triclocarban powder is stable.

Flammability (F) Score (vH, H, M or L): L
Triclocarban 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 2014
  - Triclocarban ignited when the flame of Bunsen burner at a temperature of 950^{o}C was brought in contact with it. Thus, it was concluded that triclocarban is flammable only at high temperature of about 950^{o}C.

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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 Triclocarban (CAS #101-20-2)

TOXSERVICES
TOXICOLOGY RISK ASSESSMENT CONSULTING

GREEN SCREEN FOR SAFER CHEMICALS

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	Triclocarban	101-20-2	L	L	M	L	M	L	L	M	DG	DG	L	DG	M	M	vH	vH	H	L	L	L

Table 3: Hazard Summary Table

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

Table 4

Chemical Name	Preliminary GreenScreen® Benchmark Score
Triclocarban	2

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

Table 6

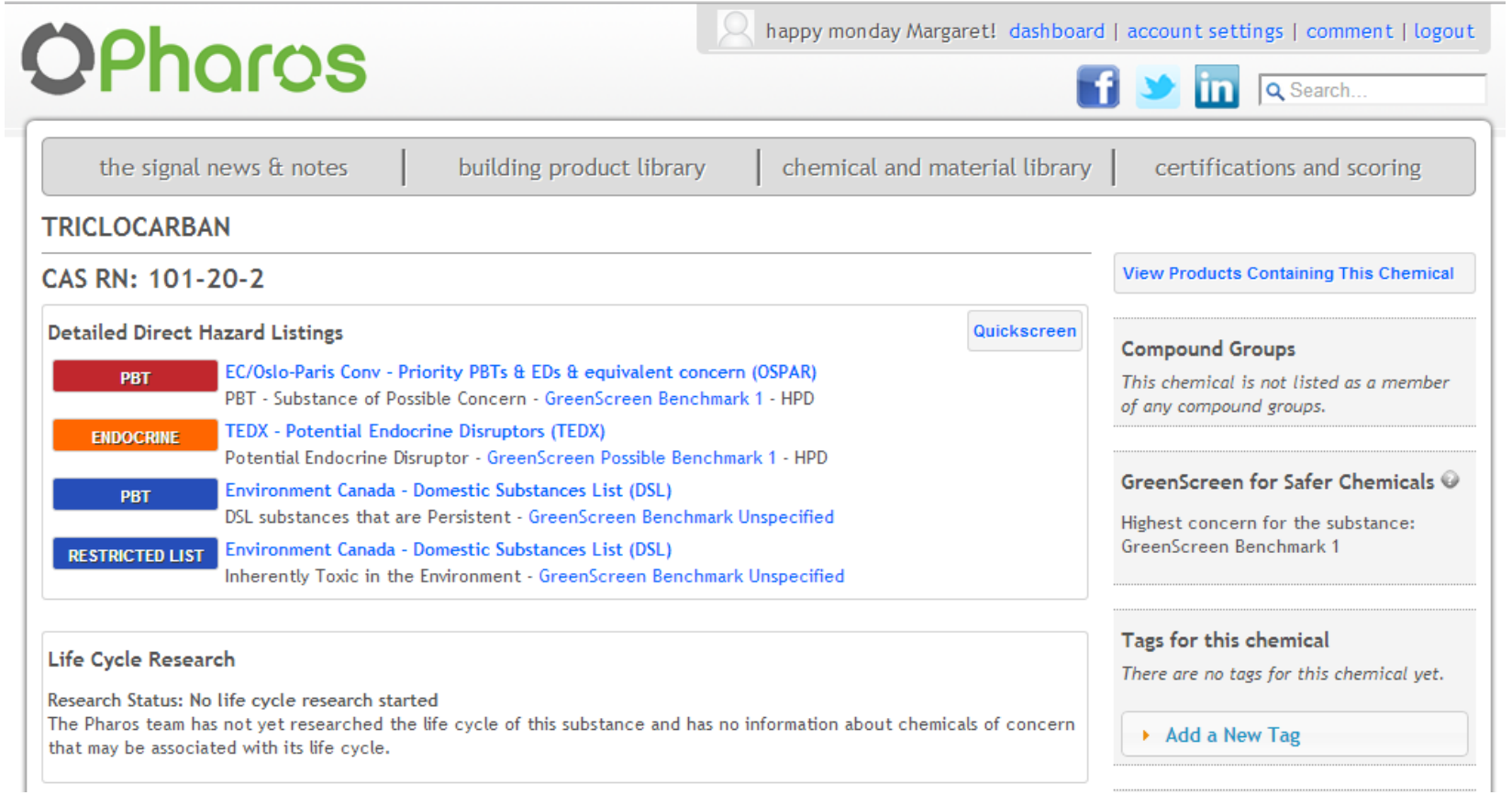
Chemical Name	Final GreenScreen® Benchmark Score
Triclocarban	2

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

Table 5: Data Gap Assessment Table

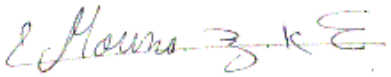
Datagap Criteria	a	b	c	d	e	f	g	h	i	j	bm4	End Result
1												
2	Yes	Yes	Yes	Yes	Yes							2
3												
4												

APPENDIX C: Pharos Output for Triclocarban (CAS #101-20-2)



Authorized Reviewers

Triclocarban GreenScreen® Evaluation Prepared By:



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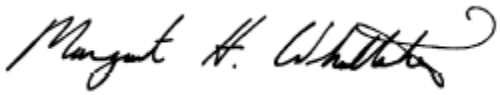
Toxicologist
ToxServices LLC

Triclocarban GreenScreen® Evaluation QC'd By:



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