



## Justification Document for the Selection of a CoRAP Substance

**Substance Name (public name):** Triclocarban

**EC Number:** 202-924-1

**CAS Number:** 101-20-2

**Authority:** French CA

**Date:** 20/03/2018

### Cover Note

This document has been prepared by the evaluating Member State given in the CoRAP update.

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## 1 IDENTITY OF THE SUBSTANCE

### 1.1 Other identifiers of the substance

**Table: Other Substance identifiers**

<b>EC name (public):</b>	Triclocarban
<b>IUPAC name (public):</b>	1-(4-chlorophenyl)-3-(3,4-dichlorophenyl)urea
<b>Index number in Annex VI of the CLP Regulation:</b>	-
<b>Molecular formula:</b>	C <sub>13</sub> H <sub>9</sub> Cl <sub>3</sub> N <sub>2</sub> O
<b>Molecular weight or molecular weight range:</b>	315.582 g/mol
<b>Synonyms:</b>	3,4,4'-trichlorocarbanilide, <i>N</i> -(4-chlorophenyl)- <i>N'</i> -(3,4-dichlorophenyl)-1-(4-chlorophenyl)-3-(3,4-dichlorophenyl)urea

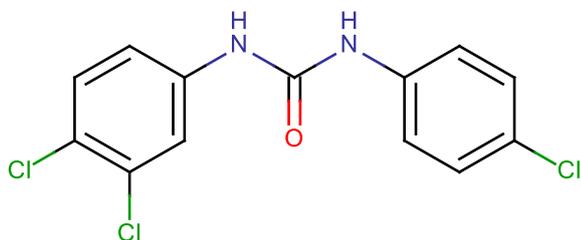
**Type of substance**

Mono-constituent

Multi-constituent

UVCB

**Structural formula:**



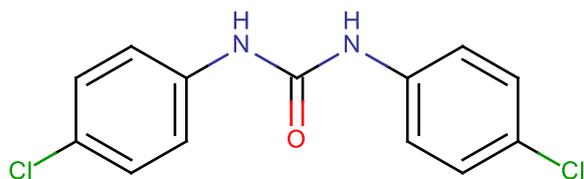
### 1.2 Similar substances/grouping possibilities

Triclocarban has a dichlorinated phenyl ring connected by an urea bond to a monochlorinated phenyl ring, and shows structural similarity to the dichlorinated carbanilide compound 1,3-Bis(4-chlorophenyl)urea. There is also structural resemblance to diuron that has a single dichlorinated phenyl ring connected by an amide bond to a dimethylamine.

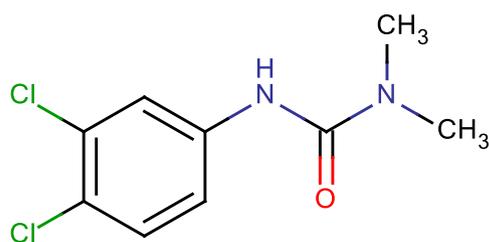
Triclocarban also shares limited structural similarity to triclosan, i.e. both substances have two chlorinated phenyl rings. But while the phenyl rings in triclocarban are connected by an urea bond, in triclosan they are connected by an ether bond. Furthermore, triclosan contains an additional hydroxyl group, and the chlorines are located at different positions compared to triclocarban.

**Table: Structurally similar substance (1)**

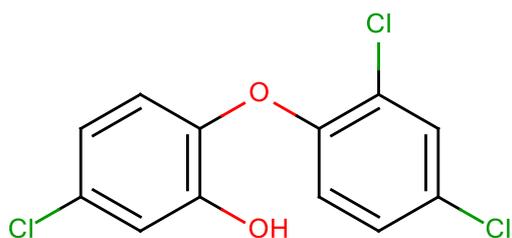
<b>EC number:</b>	-
<b>EC name (public):</b>	-
<b>CAS number:</b>	1219-99-4
<b>CAS name (public):</b>	
<b>IUPAC name (public):</b>	1,3-Bis(4-chlorophenyl)urea
<b>Index number in Annex VI of the CLP Regulation:</b>	-
<b>Molecular formula:</b>	C <sub>13</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>2</sub> O
<b>Molecular weight or molecular weight range:</b>	281.137 g/mol
<b>Synonyms:</b>	<i>Carbanilide, 4,4'-dichloro-</i>

**Structural formula:****Table: Structurally similar substance (2)**

<b>EC number:</b>	206-354-4
<b>EC name (public):</b>	Diuron
<b>CAS number:</b>	330-54-1
<b>CAS name (public):</b>	
<b>IUPAC name (public):</b>	3-(3,4-dichlorophenyl)-1,1-dimethylurea
<b>Index number in Annex VI of the CLP Regulation:</b>	-
<b>Molecular formula:</b>	C <sub>9</sub> H <sub>10</sub> Cl <sub>2</sub> N <sub>2</sub> O
<b>Molecular weight or molecular weight range:</b>	233.095 g/mol
<b>Synonyms:</b>	<i>n'-(3,4-dichlorophenyl)-n,n-dimethylurea Urea, N'-(3,4-dichlorophenyl)-N,N-dimethyl-</i>

**Structural formula:****Table: Structurally similar substance (3)**

<b>EC number:</b>	222-182-2
<b>EC name (public):</b>	Triclosan
<b>CAS number:</b>	3380-34-5
<b>CAS name (public):</b>	
<b>IUPAC name (public):</b>	
<b>Index number in Annex VI of the CLP Regulation:</b>	-
<b>Molecular formula:</b>	C <sub>12</sub> H <sub>7</sub> Cl <sub>3</sub> O <sub>2</sub>
<b>Molecular weight or molecular weight range:</b>	289.542 g/mol
<b>Synonyms:</b>	<i>2,4,4'-trichloro-2'-hydroxy-diphenyl-ether</i> <i>5-chloro-2-(2,4-dichlorophenoxy)phenol</i> <i>phenol, 5-chloro-2-(2,4-dichlorophenoxy)-</i>

**Structural formula:**

## 2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

**Table: Completed or ongoing processes**

RMOA	<input checked="" type="checkbox"/> Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	<input type="checkbox"/> Compliance check, Final decision
		<input type="checkbox"/> Testing proposal
		<input type="checkbox"/> CoRAP and Substance Evaluation
	Authorisation	<input type="checkbox"/> Candidate List
		<input type="checkbox"/> Annex XIV
	Restriction	<input type="checkbox"/> Annex XVII <sup>1</sup>
Harmonised C&L	<input type="checkbox"/> Annex VI (CLP) (see section 3.1)	
Processes under other EU legislation	<input type="checkbox"/> Plant Protection Products Regulation Regulation (EC) No 1107/2009	
	<input checked="" type="checkbox"/> Biocidal Product Regulation Regulation (EU) 528/2012 and amendments	
Previous legislation	<input type="checkbox"/> Dangerous substances Directive Directive 67/548/EEC (NONS)	
	<input type="checkbox"/> Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)	
(UNEP) Stockholm convention (POPs) <small>Protocol</small>	<input type="checkbox"/> Assessment	
	<input type="checkbox"/> In relevant Annex	
Other processes / EU legislation	<input checked="" type="checkbox"/> Other (provide further details below)	

<sup>1</sup> Please specify the relevant entry.

Further details	<p>Triclocarban has been included on the Public Activities Coordination Tool (PACT) on 11 march 2016 by the French Competent Authority, and a risk management option analysis (RMOA) is under development with the concern being the potential endocrine disrupting properties of the substance.</p> <p>Triclocarban is listed under reference number 100 in Annex III and reference number 23 in Annex V of regulation (EC) No 1223/2009 on cosmetic products. It is allowed for use as a preservative and use other than as a preservative with the maximum concentrations in ready for use preparation being 1.5 and 0.2%, respectively. For both uses the purity criteria are <math>\leq 1</math>ppm of 3,3',4,4'-tetrachloroazobenzene and 3,3',4,4'-tetrachloroazoxy-benzene. A Scientific Committee on Consumer Products (SCCP) opinion has been adapted for triclocarban on 1 June 2005 for other uses than as a preservative (SCCP/0851/04). It has been concluded that use of triclocarban for non-preservative purposes in cosmetic rinse-off hand and body care products up to a maximum concentration of 1.5% does not pose a direct risk to the health of the consumer. However, the opinion did draw the Commission's attention to the possible effects of triclocarban to the environment and, subsequently, on human health from such environmental contaminations.</p> <p>The triclocarban consortium submitted in 2002 to the U.S. EPA High Production Volume (HPV) Challenge Program data on physical-chemical properties, human health, and environmental toxicity.</p> <p>In 2010, triclocarban was being considered for inclusion in the California Environmental Contaminant Biomonitoring Program (CECBP) by the Scientific Guidance Panel (SGP) Biomonitoring California . It was not included.</p>
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### 3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

#### 3.1 Classification

##### 3.1.1 Harmonised Classification in Annex VI of the CLP

There is no harmonised Classification and Labelling for the substance.

##### 3.1.2 Self classification

There are notifications for triclocarban in the C&L inventory (C&L Inventory was accessed on August 2017). The following hazard classes have been notified among the aggregated self classifications in the C&L Inventory:

- Aquatic Acute 1 with hazard statement H400: Very toxic to aquatic life.
- Aquatic Chronic 1 with hazard statement H410: Very toxic to aquatic life with long lasting effects.
- Skin Irrit. 2 with hazard statement H315: Causes skin irritation.
- Eye Irrit. 2 with hazard statement H319: Causes serious eye irritation.

### 3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

Currently there is no proposal for Harmonised Classification and Labelling in Annex VI of the CLP.

## 4 INFORMATION ON (AGGREGATED) TONNAGE AND USES<sup>2</sup>

### 4.1 Tonnage and registration status

**Table: Tonnage and registration status**

<b>From ECHA dissemination site (accessed in August 2017)*</b>		
<input checked="" type="checkbox"/> Full registration(s) (Art. 10)	<input type="checkbox"/> Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
<input type="checkbox"/> 1 - 10 tpa	<input type="checkbox"/> 10 - 100 tpa	<input checked="" type="checkbox"/> 100 - 1000 tpa
<input type="checkbox"/> 1000 - 10,000 tpa	<input type="checkbox"/> 10,000 - 100,000 tpa	<input type="checkbox"/> 100,000 - 1,000,000 tpa
<input type="checkbox"/> 1,000,000 - 10,000,000 tpa	<input type="checkbox"/> 10,000,000 - 100,000,000 tpa	<input type="checkbox"/> > 100,000,000 tpa
<input type="checkbox"/> <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		<input type="checkbox"/> Confidential
1 joint submission which include 2 registrants.		

\*the total tonnage band has been calculated by excluding the intermediate uses, for details see the Manual for Dissemination and Confidentiality under REACH Regulation (section 2.6.11):

[https://echa.europa.eu/documents/10162/22308542/manual\\_dissemination\\_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0](https://echa.europa.eu/documents/10162/22308542/manual_dissemination_en.pdf/7e0b87c2-2681-4380-8389-cd655569d9f0)

### 4.2 Overview of uses

Triclocarban is an antibacterial agent. The substance is used as such. At industrial sites it is used as intermediate, for the formulation/mixing of cosmetics and personal care products, and automated application of water-borne adhesives. Consumer uses include use in coatings and paints, thinners, paint removes, fillers, putties, plasters, modelling clay, finger paints, ink and toners, pharmaceuticals, washing and cleaning products (including solvent based products), laboratory

<sup>2</sup> Please provide here the date when the dissemination site was accessed.

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reagent, air care products, and cosmetics, personal care products. Furthermore, it is used for service life of cured stone, plaster, cement, glass and ceramic articles.

**Table: Uses**

**Part 1:**

<input checked="" type="checkbox"/> Manufacture	<input checked="" type="checkbox"/> Formulation	<input checked="" type="checkbox"/> Industrial use	<input type="checkbox"/> Professional use	<input checked="" type="checkbox"/> Consumer use	<input checked="" type="checkbox"/> Article service life	<input type="checkbox"/> Closed system
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**Part 2:**

	<b>Use(s)</b>
<b>Uses as intermediate</b>	<ul style="list-style-type: none"> <li>- PROC 3: Use in closed batch process (synthesis or formulation)</li> <li>- PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact)</li> <li>- PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities</li> <li>- PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing)</li> </ul>
<b>Formulation</b>	<ul style="list-style-type: none"> <li>- PROC 1: Use in closed process, no likelihood of exposure</li> <li>- PROC 2: Use in closed, continuous process with occasional controlled exposure</li> <li>- PROC 3: Use in closed batch process (synthesis or formulation)</li> <li>- PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises</li> <li>- PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact)</li> <li>- PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities</li> <li>- PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities</li> <li>- PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing)</li> <li>- PROC 14: Production of preparations or articles by tableting, compression, extrusion, pelletisation</li> <li>- PROC 15: Use as laboratory reagent</li> <li>- PROC 15: Use as laboratory reagent</li> </ul>
<b>Uses at industrial sites</b>	<ul style="list-style-type: none"> <li>- PROC 2: Use in closed, continuous process with occasional controlled exposure</li> <li>- PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises</li> <li>- PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact)</li> <li>- PROC 7: Industrial spraying</li> <li>- PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities</li> <li>- PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing)</li> <li>- PROC 10: Roller application or brushing</li> </ul>

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<b>Uses by professional workers</b>	no
<b>Consumer Uses</b>	<ul style="list-style-type: none"> <li>- PC 3: Air care products</li> <li>- PC 9a: Coatings and paints, thinners, paint removes</li> <li>- PC 9b: Fillers, putties, plasters, modelling clay</li> <li>- PC 9c: Finger paints</li> <li>- PC 18: Ink and toners</li> <li>- PC 29: Pharmaceuticals</li> <li>- PC 35: Washing and cleaning products (including solvent based products)</li> <li>- PC 39: Cosmetics, personal care products</li> </ul>
<b>Article service life</b>	<ul style="list-style-type: none"> <li>- AC 4: Stone, plaster, cement, glass and ceramic articles</li> </ul>

**Part 3: There is high potential for exposure of**

<input checked="" type="checkbox"/> Humans	<input checked="" type="checkbox"/> Environment
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## 5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

### 5.1. Legal basis for the proposal

- Article 44(2) (refined prioritisation criteria for substance evaluation)
- Article 45(5) (Member State priority)

### 5.2. Selection criteria met (why the substance qualifies for being in CoRAP)

- Fulfils criteria as CMR/ Suspected CMR
- Fulfils criteria as Sensitiser/ Suspected sensitiser
- Fulfils criteria as potential endocrine disruptor
- Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB
- Fulfils criteria high (aggregated) tonnage (*tpa* > 1000)
- Fulfils exposure criteria
- Fulfils MS's (national) priorities (SNPE<sup>3</sup> 2016)

### 5.3. Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR <input type="checkbox"/> C <input type="checkbox"/> M <input type="checkbox"/> R	Suspected CMR <sup>4</sup> <input type="checkbox"/> C <input type="checkbox"/> M <input checked="" type="checkbox"/> R	<input checked="" type="checkbox"/> Potential endocrine disruptor
<input type="checkbox"/> Sensitiser	<input type="checkbox"/> Suspected Sensitiser <sup>4</sup>	
<input type="checkbox"/> PBT/vPvB	<input type="checkbox"/> Suspected PBT/vPvB <sup>4</sup>	<input type="checkbox"/> Other (please specify below)
Exposure/risk based concerns		
<input checked="" type="checkbox"/> Wide dispersive use	<input type="checkbox"/> Consumer use	<input type="checkbox"/> Exposure of sensitive populations
<input type="checkbox"/> Exposure of environment	<input type="checkbox"/> Exposure of workers	<input type="checkbox"/> Cumulative exposure
<input type="checkbox"/> High RCR	<input type="checkbox"/> High (aggregated) tonnage	<input type="checkbox"/> Other (please specify below)

<sup>3</sup> French Annual National Strategy for Endocrine Disruptors

<sup>4</sup> CMR/Sensitiser: known carcinogenic and/or mutagenic and/or reprotoxic properties/known sensitising properties (according to CLP harmonized or registrant self-classification or CLP Inventory)  
Suspected CMR/Suspected sensitiser: suspected carcinogenic and/or mutagenic and/or reprotoxic properties/suspected sensitising properties (not classified according to CLP harmonized or registrant self-classification)  
Suspected PBT: Potentially Persistent, Bioaccumulative and Toxic

Wide dispersive use and exposure of the environment are likely, as triclocarban is amongst others used in consumer products such as paints, cosmetics or cleaning and personal care products.

Concerning the reprotoxicity of the substance, Triclocarban induced adverse effects on reproductive organs especially on male one like on the ventral prostate or the seminal vesicles in a study performed in rats exposed during 10 days (Duleba *et al.*, 2011). Moreover effects on testes were observed in chronic studies in rats at 250 mg/kg bw/day (Monsanto, 1981) and a degeneration of the seminiferous tubules was observed following an exposure to 3000 to 10 000 ppm of TCC in rats (Wright *et al.*, 1975). Therefore a concern for reprotoxicity is raised and need to be further clarified.

In the current state of the knowledge and with regard to the guidelines of the OECD (OECD, on 2012) for the evaluation of ED substances, it is considered that on the basis of the toxicological and ecotoxicological data provided in the registration dossier, there is no sufficient information to be able to identify potential ED effects. The results observed suggest that Triclocarban has an endocrine disruptor character with an important level of evidence: Triclocarban could alter the biosynthesis of the thyroid hormones by modulating the contribution in iodine in thyreocytes in certain conditions. Triclocarban has the capacity of interfering with the receptor AhR and can enhance testosterone dependent induction of luciferase gene expression and have weak estrogenic activities. These results suggests that Triclocarban has an endocrine disruptor character with an important level of evidence because there is robust information on the ED effects such as androgen or thyroid or steroidogenesis *in vitro* and some results on carcinogenicity on mammary gland *in vitro* potentially mediated by an ED mode of action. Nevertheless, due to the lack of detailed information and in the absence of known adverse effects, it is not possible to conclude on the ED properties of this substance.

In order to have sufficient information to link the mode of action observed *in vitro* with adverse effects, a reprotoxicity assay could be recommended in order to clarify the concern for for the possible ED properties of the triclocarban. FR would also like to clarify the promoting effect of Triclocarban on the bacterial resistance.

Regarding the ED potential in the environmental organisms, one study indicates that Triclocarban could have a potential androgenic activity on fish as it enhances AR-mediated response to a well-know androgen (Trenbolone). Other studies suggest that Triclocarban has both estrogenic and androgenic activity through regulation of *vtg* and *ar* gene expression and might impact steroidogenesis through decline in cholesterol levels and inhibition of *star* gene expression in fish. Finally, chronic effect on reproduction were observed (increased number of embryos) in New Zealand mudsail after Triclocarban treatment. This significant increase of number of embryos has been previously found in experiments with exogenous estrogenic ED compounds (BPA, octylphenol, nonylphenol, ethynylestradiol).

However, concerning the environmental ED potential, supplementary data conducted according to recognized guidelines would allow to confirm or invalidate the proposed assumptions.

#### 5.4. Preliminary indication of information that may need to be requested to clarify the concern

<input checked="" type="checkbox"/> Information on toxicological properties	<input type="checkbox"/> Information on physico-chemical properties
<input type="checkbox"/> Information on fate and behaviour	<input type="checkbox"/> Information on exposure

<input type="checkbox"/> Information on ecotoxicological properties	<input type="checkbox"/> Information on uses
<input checked="" type="checkbox"/> Information ED potential	<input type="checkbox"/> Other (provide further details below)
<p>Based on a preliminary examination of the available data, and in order to be able to link the mode of action observed <i>in vitro</i> with adverse effect(s), a reprotoxicity assay such as an EOGRTS may be requested in order to clarify the concern about ED properties of triclocarban.</p> <p>Concerning the environmental ED potential, supplementary data with recognized guidelines would allow to confirm or invalidate the ED concerns.</p>	

### 5.5. Potential follow-up and link to risk management

<input checked="" type="checkbox"/> Harmonised C&L	<input type="checkbox"/> Restriction	<input checked="" type="checkbox"/> Authorisation	<input type="checkbox"/> Other (provide further details)
<p>When the reprotox and ED concerns would be clarified different follow-up may be foreseen.</p>			