Justification Document for the Selection of a CoRAP Substance

Substance Name (public name):	Dicyclohexyl phthalate (DCHP)
EC Number:	201-545-9
CAS Number:	84-61-7
Authority:	Swedish Chemicals Agency
Date:	21/03/2017

Cover Note

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

1 IDENTITY OF THE SUBSTANCE

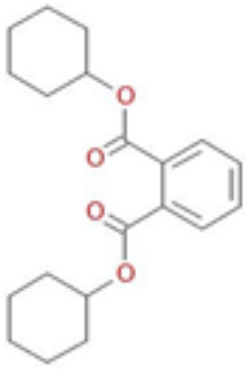
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	Dicyclohexyl phthalate
IUPAC name (public):	Dicyclohexyl phthalate
Index number in Annex VI of the CLP Regulation:	607-719-00-4 (this index number is included in the 9th ATP)
Molecular formula:	C20H26O4
Molecular weight or molecular weight range:	330.418
Synonyms:	1,2-Benzenedicarboxylic acid Dicyclohexylester DCHP

Type of substance ☒ Mono-constituent ☐ Multi-constituent ☐ UVCB

Structural formula:

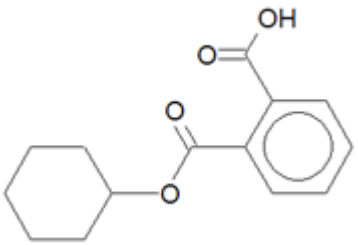


Other relevant information about substance composition

Table: Degradation (transformation) product or metabolite

EC number:	N.A.
EC name (public):	N.A
CAS number:	7517-36-4
CAS name (public):	1,2-Benzenedicarboxylic acid, 1-cyclohexyl ester
IUPAC name (public):	N.A.
Index number in Annex VI of the CLP Regulation:	N.A.
Molecular formula:	C14H16O4
Molecular weight or molecular weight range:	248.3
Synonyms:	Monocyclohexyl phthalate MCHP

Structural formula:



1.2 Similar substances/grouping possibilities

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☐ Compliance check, Final decision
		☐ Testing proposal, Final decision
		☐ CoRAP and Substance Evaluation

	Authorisation	☒ Candidate List
		☐ Annex XIV
	Restri -ction	☐ Annex XVII
Harmonised C&L		☒ Annex VI (CLP) (see section 3.1)
Processes under other EU legislation		☐ Plant Protection Products Regulation Regulation (EC) No 1107/2009
		☐ Biocidal Product Regulation Regulation (EU) 528/2012 and amendments
Previous legislation		☐ Dangerous substances Directive Directive 67/548/EEC (NONS)
		☐ Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)
(UNEP) Stockholm convention (POPs Protocol)		☐ Assessment
		☐ In relevant Annex
Other processes / EU legislation		☐ Other (provide further details below)

Sweden in collaboration with Denmark prepared an Annex XV dossier proposing that DCHP should be listed on the Candidate list because it fulfils the criteria of REACH article 57c due to its reproductive toxicity effects and article 57f for both health and the environment due to its endocrine disrupting properties. The proposal was discussed at MSC 48, 6-10 June 2016. MSC supported that DCHP fulfils the criteria for 57c (repro). However, due to differing views among the MSC members regarding 57f, ED human health, this part of the proposal was referred to the Commission. In relation to the part concerning the environment, the proposal has been prepared on the basis of experimental data on mode of action and adverse effects in rodents that were considered relevant for mammals in general. Furthermore, some additional data on potential ED effects in fish were presented, but considered limited and not sufficiently robust. The proposal for ED Env was withdrawn because the existing data concerning potential endocrine disrupting effects was considered not sufficient to conclude/agree that DCHP has endocrine disrupting properties for which there is evidence of probable serious adverse effects to the environment giving rise to equivalent level of concern.

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

DCHP was included in the 9th ATP to CLP, which was agreed at the 44th meeting of the REACH Committee 3-4 February 2016 and subsequently included in COMMISSION REGULATION (EU) 2016/1179 of 19 July 2016.

Table: Harmonised classification

Index No	International Chemical Identification	EC No	CAS No	Classification		Spec. Conc. Limits, M-factors	Notes
				Hazard Class and Category Code(s)	Hazard statement code(s)		
607-719-00-4	Dicyclohexyl phthalate	201-545-9	84-61-7	Repr. 1B Skin Sens. 1	H360D H317		

3.1.2 Self classification

- In the registration:

  Skin Sens. 1 H 317
  Repr. 2 H 361
  Aquatic Chronic 3 H 412

- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:

  Skin Irrit. 2 H 315
  Eye Irrit. 2 H 319
  STOT SE 3 H 335
  Not classified

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[1]

4.1 Tonnage and registration status

Table: Tonnage and registration status

From ECHA dissemination site		
☒ Full registration(s) (Art. 10)	☐ Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
☐ 1 – 10 tpa	☐ 10 – 100 tpa	☒ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	☐ 100,000 – 1,000,000 tpa
☐ 1,000,000 – 10,000,000 tpa	☐ 10,000,000 – 100,000,000 tpa	☐ > 100,000,000 tpa
☐ <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		☐ Confidential
The substance has three active registrations and one joint submission.		

4.2 Overview of uses

DCHP is used for the manufacturing of e.g. plastisol, PVC, rubber and plastic articles, sealant compounds and textile printing and as phlegmatizer and dispersing agent for formulations of organic peroxides.

Plastisol and organic peroxides are used at industrial sites and by professional workers.

Consumer uses of products containing DCHP includes polymer preparations and compounds, adhesives and sealants, coating products, fillers, putties, plasters, modelling clay, finger paints, non-metal-surface treatment products, inks and toners, polishes and waxes and textile treatment products and dyes.

Table: Uses

Part 1:

☒ Manufacture	☒ Formulation	☒ Industrial use	☒ Professional use	☒ Consumer use	☒ Article service life	☐ Closed system

[1] *The dissemination site was accessed 7 March 2017*

Part 2:

	Use(s)
Uses as intermediate	
Formulation	Co-plasticizer for PVC, rubber and plastic compunds, phlegmatizer and dispersion agent , sealant compounds and textile printing
Uses at industrial sites	End-use of plastisol, organic peroxides Manufature of PVC, rubber and plastic articles
Uses by professional workers	End-use of plastisol, end/use stage of organic peroxide
Consumer Uses	Plastisol, organic peroxide
Article service life	PVC, rubber, plastic articles as plastisol

Part 3: There is high potential for exposure of

☒ Humans	☒ 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 disrupter

☐ Fulfils criteria as PBT/vPvB / Suspected PBT/vPvB

☐ Fulfils criteria high (aggregated) tonnage (*tpa > 1000*)

☒ Fulfils exposure criteria

☒ Fulfils MS's (national) priorities

5.3 Initial grounds for concern to be clarified under Substance Evaluation

Hazard based concerns		
CMR ☐ C ☐ M ☐ R	Suspected CMR[1] ☐ C ☐ M ☐ R	☒ Potential endocrine disruptor
☐ Sensitiser	☐ Suspected Sensitiser[2]	
☐ PBT/vPvB	☐ Suspected PBT/vPvB[1]	☐ Other (please specify below)

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[2] 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

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Exposure/risk based concerns		
☒ Wide dispersive use	☐ Consumer use	☐ Exposure of sensitive populations
☒ Exposure of environment	☐ Exposure of workers	☐ Cumulative exposure
☐ High RCR	☐ High (aggregated) tonnage	☐ Other (please specify below)

Mammalian data clearly indicate that DCHP has endocrine disrupting properties. DCHP has been shown to adversely affect the endocrine system of mammals primarily through *in vivo* findings on reduced fetal testosterone production. These findings are further substantiated by mechanistic findings of inhibitory effects on enzymes in the steroidogenic biosynthesis pathway. The spectrum of effects observed in rats include increased areola mammae retention, decreased anogenital distance, prolonged preputial separation, genital malformations associated with small testis, signs of reduced sperm quality, atrophic tubules in prostate, prostatic intraepithelial neoplasia and testicular changes including tubular atrophy.

However, very limited information is available on ED relevant effects in aquatic species. Only two relevant studies have been identified in which endocrine relevant parameters are included, both of which were conducted by the Japanese Ministry of the Environment (MoE). Only a brief overview of the results from these studies has been published in English (Dang et al. 2011) and hence, the original unpublished Japanese study reports have been consulted in order to evaluate many important parameters and to establish validity of the two studies.

In a 21-day fish screening assay on Medaka (Oryzias latipes) no vitellogenin induction in male fish was identified. The test was performed with solvent control, control and five exposure groups of 17.9, 38.2, 87.2, 188 and 388 µg/L (average measured concentrations).

In addition, a partial life cycle test has been conducted with Medaka (Oryzias latipes). The test was conducted with 60 fish in each exposure group consisting of control, solvent control, 0.429, 1.41, 4.39, 13.3 and 35.8 µg/L (average measured concentrations). No statistically significant effects were recorded on hatchability, time to hatching, mortality and hepasomatic index. A statistically significant increase in the gonadosomatic index was observed for the highest exposure group. In addition, the sex ratio was statistically significant skewed towards more males at the test concentration of 1.41 µg/L but not at other test concentrations and one of ten male fish in the highest exposure group developed testis-ova, an intersex condition characterized by both testicular and ovarian tissue in the gonad. The medaka is completely dioecious in nature and emergence of testicular eggs in medaka is only known to be caused by exposure to estrogen agonist or anti-androgenic substances. However, the finding of testis-ova in one fish is not considered sufficiently robust to make a firm conclusion. Finally, a statistically significant effect on vitellogenin induction in male fish was observed at the concentration of 4.39 µg/L but not at higher or lower concentrations.

Exposure from DCHP to the environment can be expected from all life cycle stages. DCHP is frequently found in food items and indoor air. Little environmental monitoring data are available but DCHP has been detected in e.g. municipal sewage treatment effluent (Nakada N et al (2004); Berset JD, Etter-Holzer R (2001)) and soil, (Liu H et al (2010)).The available in vitro data as well as in vivo data on rodents indicate that DCHP has endocrine disrupting properties. However, the ecotox database is poor with only two studies on fish of which one indicates endocrine mediated effects but lacks dose response for the observed effects. Further studies are therefore needed to judge whether DCHP is an endocrine

disrupter in fish.

If, in addition to the listing on the candidate list based on Reach article 57c due to its reprotoxicity, DCHP is also identified as an environmental ED and consequently also is listed according to article 57f this would lead to improved risk management measures. Assessment of risk for the environment would be added to the scope for authorisation. If it is considered that determination of a threshold for endocrine effects is not possible, granting of authorisations would be based on article 60 (4) meaning that authorisation may only be granted if it is shown that socio-economic benefits outweigh the risk arising from the use of the substance and if there are no suitable alternative substances or technologies.

The risk management option of listing a substance on the candidate list both for 57c (repro) and 57f (ED env) has so far been used for Diethylhexylphthalate (EC 204-211-0).

5.4 Preliminary indication of information that may need to be requeste to clarify the concern

☐ Information on toxicological properties	☐ Information on physico-chemical properties
☐ Information on fate and behaviour	☐ Information on exposure
☒ Information on ecotoxicological properties	☐ Information on uses
☒ Information on ED potential	☐ Other (provide further details below)

In order to clarify the endocrine disrupting effects of DCHP, further long term studies on aquatic organisms designed to explore the possible ED effects may need to be requested.

5.5 Potential follow-up and link to risk management

☐ Harmonised C&L	☐ Restriction	☒ Authorisation	☐ Other (provide further details)

Depending on the results of the requested information Candidate listing (57f as ED for the env.) as a first step.

References:

Berset JD, Etter-Holzer R; J AOAC Int 84: 383-91 (2001)

Dang, Z., Li, K., Yin, H., Hakkert, B., & Vermeire, T. (2011): Endpoint sensitivity in fish endocrine disruption assays: regulatory implications. Toxicology letters, 202(1), 36-46.

Liu H et al; Chemosphere 78: 382-8 (2010)

Nakada N et al; Environ Toxicol Chem 23: 2807-15 (2004)