Justification Document for the Selection of a CoRAP Substance

Substance Name (public name):	Phenol, isopropylated, phosphate (3:1)
EC Number:	273-066-3
CAS Number:	68937-41-7
Authority:	The Netherlands
Date:	18/03/2020

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

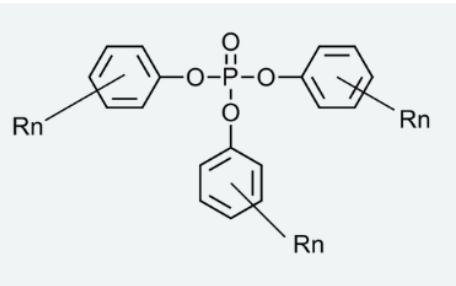
1.1 Other identifiers of the substance

Table: Other Substance identifiers

EC name (public):	Phenol, isopropylated, phosphate (3:1)
IUPAC name (public):	Diphenyl 4-(propan-2-yl)phenyl phosphate phenyl bis[4-(propan-2-yl)phenyl] phosphate triphenyl phosphate tris[4-(propan-2-yl)phenyl] phosphate
Index number in Annex VI of the CLP Regulation:	-
Molecular formula:	CXHYO4P X and Y are variable dependent on the molecular component.
Molecular weight or molecular weight range:	-
Synonyms:	Trade names: Durad® Lubad® Phosflex 31L Phosflex 41L Reofos® Reolube® Roflex Syn-o-ad 9578

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

Structural formula:



R = isopropyl; n = 0, 1, 2 or 3

1.2 Similar substances/grouping possibilities

Phenol, isopropylated, phosphate (3:1) is part of a group of triphenylphosphate derivatives. This group is under attention due to a broad concern with respect to reproduction, endocrine disruption, adverse effects after prolonged exposure, and potential PBT/vPvB properties. The manual screening performed by the Netherlands aimed to determine if any group members are left out of regulatory action, especially those with clear concerns for the summarised endpoints. Phenol, isopropylated, phosphate (3:1), EC no. 273-066-3, was identified as the group member with the highest concern with respect to neurotoxicity, reprotoxicity, endocrine disruption and PBT/vPvB properties. For this substance thus far only testing proposal evaluations and a compliance check has been performed. Therefore, phenol, isopropylated, phosphate (3:1) is selected as the most appropriate candidate for CoRAP entry.

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☒ Compliance check
		☒ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restriction	☐ Annex XVII[1]
CLH	☐ 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 67/548/EEC (NONS)	
	☐ Existing Substances Regulation 793/93/EEC (RAR/RRS)	
(UNEP) Stockholm convention (POPs Protocol)	☐ Assessment	
	☐ In relevant Annex	
Other processes/ EU legislation	☐ Other (provide further details below)	
Further details	A targeted compliance check was started in 2011 and terminated after a dossier update. Three Testing Proposals have been submitted, of which two are concluded. The Decision on the third Testing Proposal was sent to the Registrant at 5 April 2019. The Registrant is requested to carry out an extended one-generation reproductive toxicity study (OECD TG 443) by 12 October 2021.	

[1] Please specify the relevant entry.

3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

3.1 Classification

3.1.1 Harmonised Classification in Annex VI of the CLP

Not classified.

3.1.2 Self classification

- In the registration:

  Repr. 2 (H361)

  STOT RE 2 (H373)

  Aquatic Chronic 4 (H413)

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

  Skin Sens. 1 (H317)

  Skin Sens. 1B (H317)

  Aquatic Acute 1 (H400)

  Aquatic Chronic 1 (H410)

  Aquatic Chronic 2 (H411)

3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

No proposals.

4 INFORMATION ON (AGGREGATED) TONNAGE AND USES[2]

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
Joint submission.		

***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

4.2 Overview of uses

Table: Uses

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

The substance is used, amongst others, in coatings, paints, lubricants, adhesives, heat transfer fluids and polymer mixtures.

[2] *The dissemination site was accessed in June 2019.*

5. JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

5.1. Legal basis for the proposal

☒ Article 44(2)

☐ Article 45(5)

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[3]	
☐ PBT/vPvB	☒ Suspected PBT/vPvB[1]	☐ Other (please specify below)
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)

[3] 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

Suspected PBT/vPvB

Phenol, isopropylated, phosphate (3:1) is a UVCB substance that is self-classified as Repro 2 and STOT RE 2. The persistence, bioaccumulation and toxicity potential of the constituents depends on the degree of alkylation, i.e. the amount of substituted phenols and the number of substitutes per phenol. Furthermore, the position of the substitutes (e.g. ortho, meta, para) can also play a role. As specified on ECHA's public dissemination site, phenol, isopropylated, phosphate (3:1) consists of at least 18 constituents with varying degree of isopropyl substitutions, ranging from the non-substituted triphenyl phosphate (TPP; EC No. 204-112-2) up to the completely substituted tris[2,4,6-tri(propan-2-yl)phenyl] phosphate (CAS No. 107613-54-7).

Experimental data is only available for the non-substituted constituent TPP and indicates that TPP is not a potential PBT/vPvB substance. TPP is readily biodegradable, degradable in surface water (DT_{50}: <7 d) and soil (DT_{50}: 45-78 d at 12 °C), limitedly bioaccumulative with BCF values ranging 271-420 L/kg (based on parent substance), not classifiable as CMR or STOT RE and the lowest aquatic EC_{10} amounts to 0.037 mg/L (*Oncorhynchus mykiss*; mean measured).

The UK Environmental Agencies Environmental Risk Evaluation Report (UK-RER) for isopropylphenyl diphenyl phosphate[4] reports experimental data for two substances (discussed below) that are not listed as constituents of Phenol, isopropylated, phosphate (3:1) on ECHA's public dissemination site, but that do represent some of the specified structures as they concern an unspecified isomeric mixture of ortho, meta and para isomers.

Isopropylphenyl diphenyl phosphate (IIPDP; EC No. 248-848-2) contains one isopropyl substituted phenol. This substance might be persistent in sediment with 76-87% of the applied radioactivity being extractable after 4 weeks and consisting mainly of parent substance. Bioaccumulation potential is inconclusive, as BCF values of 497 L/kg and 7188-7266 L/kg (based on parent substance) have been reported, with the higher values being obtained in a study where toxicity was observed. The lowest NOEC reported for IIPDP amounts to 0.006 mg/L (*Daphnia magna*) and the substance is considered classifiable as STOT RE.

Tris(isopropylphenyl) phosphate (EC No. 248-147-1) contains one isopropyl substitute per phenol. For this substance only experimental bioaccumulation data are available. Based on these data in the UK-RER a BCF of 1986 L/kg was estimated, which is just below the B-criterion of 2000 L/kg.

In absence of experimental data for the other constituents, PB-scores were calculated based on EPISUITE QSAR estimations and SimpleBox (v3.0) calculations. The PB-score serves as an indicator of the PBT/vPvB properties of a substance, with the P and B-scores ranging 0 to 1. A P or B-score of >0.35 indicates that the P/B criterion is met, and a score >0.5 that the vP/vB criterion is met. The calculated PB-scores ranged from 0.18 (not P) and 0.20 (not B) for TPP, up to 0.86 (v) and 0.90 (vB) for the completely substituted tris[2,4,6-tri(propan-2-yl)phenyl] phosphate. The PB-scores for the other constituents were in-between these two substances and generally increased with increased degree of alkylation.

Considering the experimental and QSAR estimated data, phenol, isopropylated, phosphate (3:1) is considered as potentially PBT/vPvB.

Concluding whether the substance is PBT/vPvB needs further evaluation and potentially generation of new information.

[4] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/290854/scho0809bqug-e-e.pdf

Potential endocrine disruptor

Toxcast assays indicate some positive results for the ER, AR and TR pathways. Ataxia and neuropathological lesions were observed in several bird studies after a single-dose treatment. Besides, ataxia and neuropathological lesions (axonal degeneration) were also reported for birds treated for 21 days, 28 days, and 91 days in sub-chronic neurotoxicity studies. Further, adverse reprotoxic effects and changes in thyroid histology were observed in male and female rats.

Toxcast and repeated dose toxicity tests indicate that the substance may have potential to interfere with EAT (estrogen, androgen, thyroid) pathways.

Further evaluation potentially including the generation of new information is needed to conclude whether the substance is an endocrine disruptor, affecting human health and/or the environment.

5.4. Preliminary indication of information that may need to be requested 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 ED potential	☐ Other (provide further details below)

Suspected PBT/vPvB
To clarify the PBT/vPvB concern for Phenol, isopropylated, phosphate (3:1) or one or more of its constituents, experimental data will be required that will substantiate the persistence (biodegradability screening and/or simulation test), bioaccumulation (BCF test) and toxicity (long-term aquatic toxicity tests) potential of the substance(s).

Potential endocrine disruptor
There is in vitro and in vivo evidence showing that the substance may interfere with EAT pathways. Further evaluation will be needed to decide on the most appropriate information, needed to confirm or remove the concern for endocrine disruption for human health or the environment.

5.5. Potential follow-up and link to risk management

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

If the substance will be identified as PBT/vPvB or as endocrine disruptor, it may be listed as a SVHC, with restriction or authorization as potential follow-up.