Justification document for the selection of a substance for CoRAP inclusion

- Update -

Substance Name (Public Name):	6,6'-di-tert-butyl-4,4'butylidenedi-m-cresol
Chemical Group:	Hindered Phenols and Bridged Alkyl Phenols
EC Number:	201-618-5
CAS Number:	85-60-9
Submitted by:	France
Date:	17/03/2015 19/03/2019 (1. update)

Cover Note

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

Table of Contents

1 IDENTITY OF THE SUBSTANCE

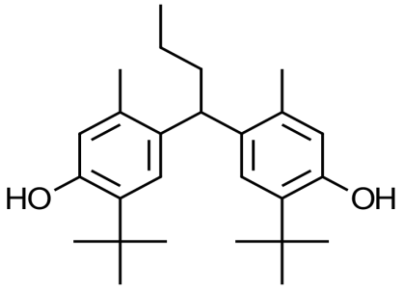
1.1 Other identifiers of the substance

Table 1: Substance identity

EC name:	6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol
IUPAC name:	4,4'-butane-1,1-diylbis(2-tert-butyl-5-methylphenol)
Index number in Annex VI of the CLP Regulation	none
Molecular formula:	$C_{26}H_{38}O_2$
Molecular weight or molecular weight range:	382.6 g/mol
Synonyms/Trade names:	• LOWINOX® 44B25 • 1,1-bis(2-methyl-4-hydroxy-5-tert-butylphenyl)butane • 2-tert-butyl-4-[1-(5-tert-butyl-4-hydroxy-2-methylphenyl)butyl]-5-methylphenol • 4,4'-Butylidenebis(6-tert-butyl-m-cresol) • 6,6''-di-tert-butyl-4,4''-butylidenedi-m-cresol • 6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol • Phenol, 4,4'-butylidenebis[2-(1,1-dimethylethyl)-5-methyl]-

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

Structural formula:



1.2 Similar substances/grouping possibilities

A grouping approach has been submitted by the registrants of phenol substances in the frame of The High Production Volume (HPV) Challenge Program[1] and published by the U.S. Environmental Protection Agency (US EPA).

The sponsor, Rubber and Plastic Additives Panel (RAPA) of the American Chemistry Council, submitted a Test Plan and Robust Summaries to US EPA for the **hindered phenols category** on December 18, 2001 as described in their document[2].

The structural similarity of the substances is based on: the hindered phenols category consists of a group of chemicals in which a molecule of phenol (hydroxybenzene) has relatively large aliphatic and/or aromatic groups positioned adjacent to the hydroxyl group (the 2-, or ortho- position). Eight substances form the hindered phenols category based on structural similarity (see Table 2), including the 6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol.

After comments formulated by the US-EPA and public consultation, the sponsor subsequently divided the hindered phenols category into two separate categories (**styrenated phenols and bridged alkyl phenols**) and two stand-alone chemicals. The sponsor submitted a test plan and robust summaries for bridged alkyl phenols category dated July 10, 2003. A the final report by US EPA (2010)[3] is available and considered as the most relevant and refined one for these substances. The structural similarity is based as follow: The bridged alkyl phenols category consists chemicals in which two molecules of mono or di-substituted alkyl (C1, C4, and/or C9) phenols are "bridged" or linked by a single atom (carbon or sulfur). The carbon atom linking the alkyl phenol groups contains hydrogen, propyl, or methyl substitutions.

Amongst the identified similar substances, several are already listed on the CoRAP for several grounds of concern including suspected PBT, ED and sensitizing properties and some have already been assessed in the frame of the PBT Expert group. This status under REACH is provided in the last column of Table 2.

From the assessment under the HPV Challenge Program, the following has been concluded by the registrants for the whole category of the bridged alkyl phenols:

- The rate of hydrolysis of bridged alkyl phenols is considered negligible;
- The rate of atmospheric photooxidation is considered rapid; however, this is not expected to be an important environmental fate process since these substances are not expected to exist in the vapor phase in the atmosphere;
- The bridged alkyl phenols are expected to have moderate persistence and a low bioaccumulation potential (except one substance CAS 79-96-9 with high bioaccumulation potential: Log Kow estimated at 7,46; BAF estimated at 7,666[4]);
- Measured LC50 to fish and aquatic invertebrates are over 0.1 mg/L.

[1] Voluntary initiative aimed at developing and making publicly available screening-level health and environmental effects information on chemicals manufactured in or imported into the United States in quantities greater than one million pounds per year

[2] Rubber and plastic Additives Panel. American Chemistry Council. Dec 2001. Hindered Phenols Category justification and Testing Rationale

[3] US-EPA. June 2010. Screening-level Hazard Characterization. Bridged Alkyl Phenol Category.

[4] U.S. EPA. 2010. Estimation Programs Interface Suite™ for Microsoft® Windows, v4.00. U.S. Environmental Protection Agency, Washington, DC, USA. Available online from: http://www.epa.gov/opptintr/exposure/pubs/episuitedl.htm as of May 10, 2010.

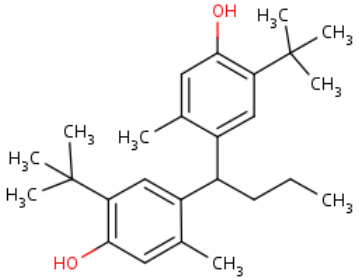
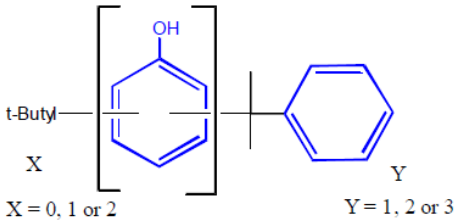
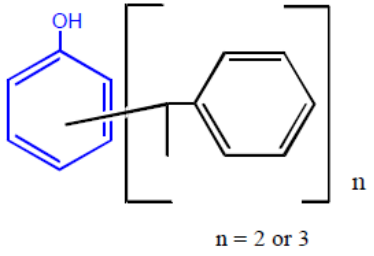
The substance Phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene (CAS 68610-51-5; EC 271-867-2), has been screened for PBT properties and:

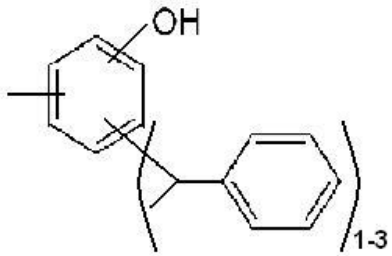
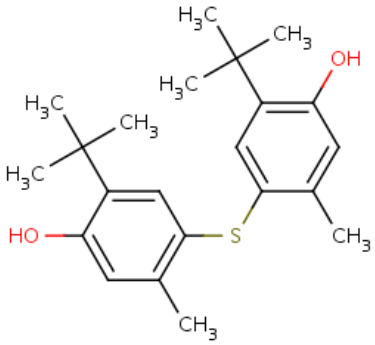
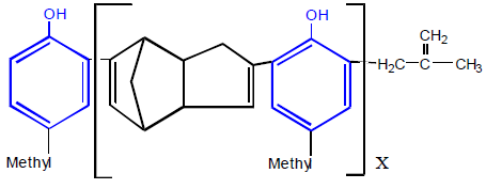
- is P and potentially vP on screening,
- is not B based on the available data but without considering the bioaccumulation potential of the constituents (expected higher) (thus no clear conclusion is yet available on the B criterion),
- is probably not T based only on acute toxicity studies.

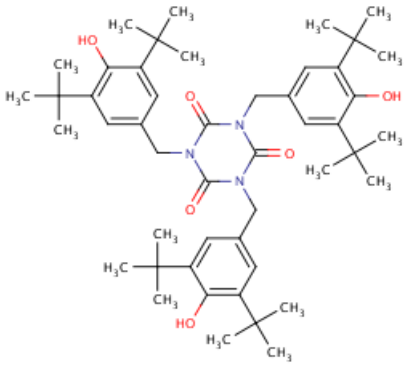
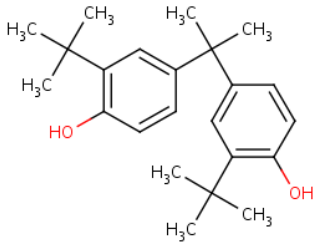
A substance evaluation under REACH for styrenated phenol (CAS 61788-44-1; EC 262-975-0) by UK was started in 2014 and is currently on-going and has been covered by an informal PBT assessment in the frame of the former TC NES PBT Working Group and the current PBT Experts Group of ECHA (confidential PBT factsheet).

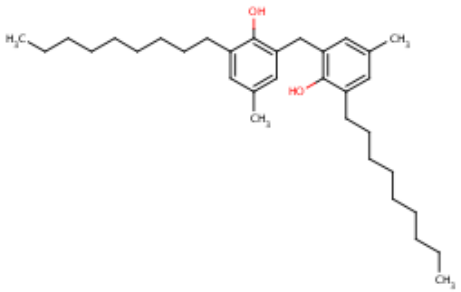
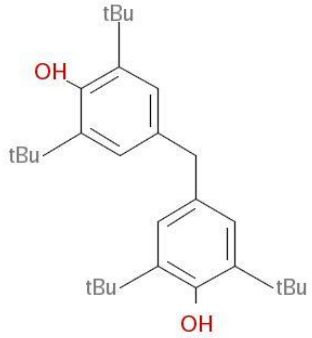
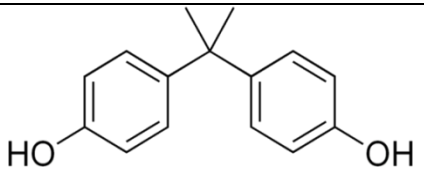
It is also noted that an additional substance, Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol (EC 700-427-9) is currently under substance evaluation by Belgium (CORAP 2013) based on initial concerns that include suspected PBT properties. In this context, the substance was discussed at the 4th PBT Expert Group of ECHA in May 2013. Although it was not included in the HPV group approach, this substance also meet the structural definition of the category and is added in table 2 for consideration.

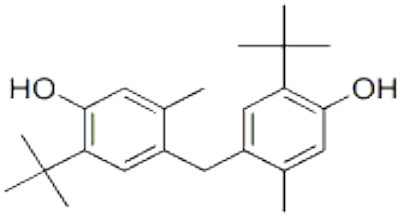
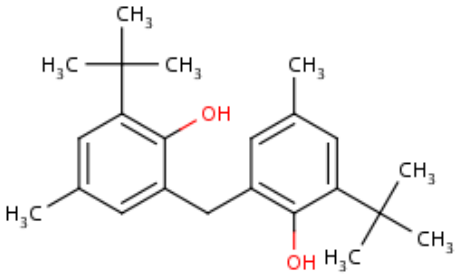
Table 2: Group approach available in the literature

Substance names	EC/CAS numbers	Structure	Category	Status under REACH
Phenol, 4,4'-butylidenebis[2-(1,1-dimethylethyl)-5-methyl- 6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol *Substance under manual screening*	201-618-5 / 85-60-9		hindered phenols category AND bridged alkyl phenols	Registered
Phenol, isobutylenated methylstyrenated	270-604-9 / 68457-74-9		hindered phenols category	Not registered
Phenol, styrenated (1) Reaction mass of 2,4,6-tris(1-phenyl-ethyl)phenol and Bis(1-phenylethyl) phenol (2)	262-975-0 / 61788-44-1 (1) 915-333-5 / NS (2)		hindered phenols category	Registered Substance subjected to transitional measures CoRAP 2014 UK (grounds for concern: Environment/Suspected PBT; Potential endocrine disruptor; Exposure/Cumulative exposure) PBT factsheet

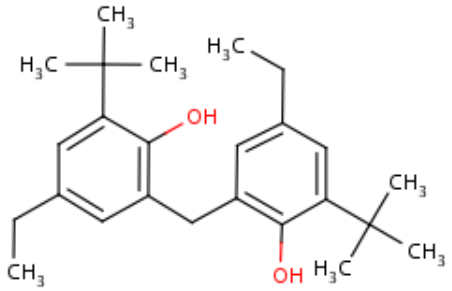
Mono- and/or di- and/or tri(1-phenylethyl)-m-cresol and p-cresol	700-427-9 / -		Not included in the HPV group approach	Registered CORAP 2013 Belgium (grounds for concern: Environment/Suspected PBT; Exposure/Wide dispersive use; Consumer use. 4th PBT EG
4,4'-Thiobis-6-(t-butyl-m-cresol) 6,6'-di-tert-butyl-4,4'-thiodi-m-cresol Phenol, 4,4'-thiobis[2-(1,1-dimethylethyl)-5-methyl-	202-525-2 / 96-69-5		hindered phenols category AND bridged alkyl phenols	Registered CoRAP 2016 Austria (grounds for concern: Human health / Suspected CMR; Sensitiser; Suspected Endocrine Disruptor; Environment/Suspected PBT; Exposure/Wide dispersive use; Consumer use)
Phenol, 4-methyl-, reaction products with dicyclopentadiene and isobutylene	271-867-2 / 68610-51-5		hindered phenols category	Registered CoRAP 2016 Spain (grounds for concern: Environment/Suspected PBT/vPvB; Exposure/Wide dispersive use, exposure of environment) PBT factsheet

1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl-)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione 1,3,5-tris(3,5-di-tert-butyl-4-hydroxybenzyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione	248-597-9 / 27676-62-6		hindered phenols category	Registered
Phenol, 4,4'-(1-methylethylidene) bis[2-(1,1-dimethylethyl)- *4,4'-isopropylidenebis(o-tert-butylphenol)*	201-239-5 / 79-96-9		hindered phenols category AND bridged alkyl phenols	Not registered

Phenol, 2,2'-methylenebis[4-methyl-6-nonyl- *2,2'-methylenebis(6-nonyl-p-cresol)*	232-092-5 / 7786-17-6		hindered phenols category AND bridged alkyl phenols	Registered
2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol	204-279-1 / 118-82-1		None identified yet	Registered Substance subjected to transitional measures CoRAP 2014 Austria (grounds for concern: Environment/Suspected PBT/vPvB; Potential endocrine disruptor; Suspected CMR, Suspected Sensitiser Exposure/Wide dispersive use, consumer use, exposure of workers, exposure of environment) PBT factsheet
Bisphenols			None identified yet	

4,4'-methylenebis(6-tert-butyl-m-cresol)	220-702-2 / 2872-08-4		According to Takahashi & Hiraga (1981)[5]	Not registered
6,6'-di-tert-butyl-2,2'-methylenedi-p-cresol 2,2'-methylenebis(6-tert-butyl-4-methylphenol) DBMC	204-327-1 / 119-47-1		According to Takahashi & Hiraga (1981)	Registered

[5] Takahashi O, Hiraga K. Effects of four bisphenolic antioxidants on lipid contents of rat liver. Toxicol Lett. 1981, Apr; 8(1-2):77-86.

6,6'-di-tert-butyl-4,4'-diethyl-2,2'-methylenediphenol	201-814-0/ 88-24-4		According to Takahashi & Hiraga (1981)	Registered

Six substances selected from table 2 are considered as relevant for assessment of the substance 6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol (named hereafter "CAS 85-60-9") by read across (i.e. compounds with two aromatic rings, with two or more t-butyl groups linked to an aromatic ring and with an OH polar group per aromatic ring).

Two of them are not registered under REACH; no or few data are thus available except from the HPV Challenge program. The substance 2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol (named hereafter TMBD) is currently under substance evaluation; a in-depth PBT assessment is already available and covered by a confidential PBT factsheet.

2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

Table 3: Completed or ongoing processes

RMOA	☐ Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	☒ Compliance check, Final decision
		☐ Testing proposal
		☐ CoRAP and Substance Evaluation
	Authorisation	☐ Candidate List
		☐ Annex XIV
	Restric -tion	☐ Annex XVII[6]
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)	

[6] Please specify the relevant entry.

	☐ 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)
Further details	

3 CLASSIFICATION AND LABELLING

3.1 Harmonised Classification in Annex VI of the CLP

No harmonised classification

3.2 Self classification

- In the registration

None (data lacking)

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

Skin irrit. 2 (H315), Eye irrit. 2 (H319), STOT RE 2 (H373), Aquatic chronic 1 (H410), 3 (H412) and Aquatic chronic 4 (H413)

3.3 Proposal for Harmonised Classification in Annex VI of the CLP

No proposal for harmonized classification in Annex Vi of the CLP

4 INFORMATION ON AGGREGATED TONNAGE AND USES

From ECHA 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 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

☒ Industrial use	☒ Professional use	☒ Consumer use	☐ Closed System

According to the draft Environmental Risk Evaluation Report: 2,2',6,6'-Tetra-tert-butyl-4,4'-methylene-diphenol (TBMD) (CAS No. 118-82-1) by the Environment Agency of England and Wales[7] TBMD is used as an antioxidant in lubricants in Europe. Same uses are expected for the whole category including 6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol, as stated by Takahashi and Hiraga (1981)[8] but since the provided PROC in the registration dossier are different, this interpretation can be questioned.

Uses at industrial sites:
Low worker exposure expected from manufacture of the substance
Low worker exposure expected from the formulation of preparations and materials (adhesives, sealants, raffia film and fibers, thermoplastics)
Workers exposure expected from the formulation of polymers and compounds and from converting

Uses by professional workers (indoor/outdoor):
Worker exposure expected from installation of articles, adhesives and sealants manipulation

Uses by consumers (indoor/outdoor):
Consumer exposure expected from manipulation of adhesives and sealants

Potential widespread uses with possible releases.

From the public report from the Rubber and Plastic Additives Panel (2001)[9], commercial applications are the following:

Hindered phenols are non-staining, non-discoloring, non- migratory additives for natural rubber, synthetic rubber, adhesives, plastics, textile fibers, cable coatings, flooring, and coated paper, as well as natural and synthetic oils. Their purpose is to prevent or greatly delay the deterioration caused by air oxidation. Using a hindered phenol antioxidant greatly extends the useful life of a transparent, translucent, white or light-colored article by preventing the formation of surface cracks, brittleness and yellowing. In oils, a hindered phenol antioxidant functions as a stabilizer, extending the useful life of the lubricating fluid by slowing the natural breakdown process and limiting the buildup of tars and residues. The overall mechanism is similar to that of the antioxidant vitamins A and E in the human body – hindered phenol antioxidants serve as free-radical scavengers. Hindered phenols are cost-effective and efficient antioxidants. Usage levels for most applications are typically within the range of 0.5 to 2%.

[7] https://echa.europa.eu/documents/10162/c69444d6-ffc8-46c0-888a-042b63f47fb2

[8] Takahashi O and Hiraga K. 1981. Effects of four bisphenolic antioxidants on lipid contents of rat liver. Toxicol Lett. 1981 Apr;8(1-2):77-86

[9] Rubber and plastic Additives Panel. American Chemistry Council. Dec 2001. Hindered Phenols Category justification and Testing Rationale

Regarding exposure: These materials are made as powders, flakes, emulsions and liquids. Product forms that minimize dust generation, coupled with the mechanized materials handling systems of the large industrial users, combine to keep exposures to minimum levels. However, during material packout at the manufacturing site and, to a lesser degree during weigh-up activities at the customer site, there is a potential for skin and inhalation exposure (nuisance dust is the primary route of worker exposure) and also dermal contact with liquid forms.

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[10]	
☐ PBT/vPvB	☒ Suspected PBT/vPvB[1]	☐ Other (please specify below)

[10] 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

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)

HH-based concern:

Substances of the category "bridged alkyl phenol" includes bisphenol A that induces adverse effects on fertility and development and presents endocrine disruption properties. In the same category, 2,2'-Methylenebis(6-tert-butyl-4-methylphenol) (CAS 119-47-1) is also reported as self-classified by some notifiers Repr 2 – H361 due to testicular effects.

Only limited information is available to evaluate the reproductive toxicant potential of 6,6'-di-tert-butyl-4,4'butylidenedi-m-cresol (screening of reproduction/developmental assay only available). Although no conclusive findings are identified in this screening assay, alerts consisting of uterine dilatation and isolated mammary adenoma are observed in the 90-day study. The endocrine disruption potential and reproductive toxicant potential of the present substance need to be further evaluated.

A prenatal developmental study has been recently included in the registration dossier and may provide relevant information on the identified concerns and will be examined in the course of the evaluation.

PBT/vPvB based oncern:

6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol was considered as not readily biodegradable (P/vP met on screening) and possibly not T based on acute toxicity data only (the reliability of the provided studies needs to be further evaluated). The substance was considered not bioaccumulative by the registrant(s) based on calculations.

Nevertheless, 6,6'-di-tert-butyl-4,4'-butylidenedi-m-cresol screens as a potential P/vP and B substance. The read-across outcome with similar substances (identified in Table 3) underlines the need to investigate further its bioaccumulation potential and then its persistence if needed. Beyond the aquatic toxicity data, the Repr. 2 status needs to be further assessed and may fulfill the T criterion of Annex XIII.

Similar substances are already scheduled for substance evaluation based on a suspected PBT concern and a group approach appears relevant; the similar substance 6,6'-di-tert-butyl-2,2'-methylenedi-p-cresol (CAS 119-47-1) has not yet identified by any IT screening but may be a good candidate too (its non-PBT status concluded by the TC NES PBT working group should indeed be revised in the light on the on-going evaluations).

Nevertheless the dossier of the substance has been recently updated and a fish dietary bioaccumulation test on this substance as well as long-term toxicity studies with fish and Daphnia are now available which will be evaluated during the evaluation of the substance. But still no simulation degradation test available and no information on any potential degradation products.

Exposure – risk based concern:

Widespread uses and possible release to the environment are suspected. No exposure assessment and estimation of release to the environment and exposure of man is provided in the registration dossiers as the substance is not considered to be PBT and does not need to be classified referring to the estimate of the registrants.

Other based concerns:

Further information on metabolites is necessary for the risk assessment process. The degradation of the substances has to be evaluated. It will be verified, if relevant metabolites are expected to be formed.

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)

5.5 Potential follow-up and link to risk management

☐ Harmonised C&L	☐ Restriction	☐ Authorisation	☐ Other (provide further details)
None at the current step, will depend on the outcome of the evaluation.			