Justification for the selection of a substance for CoRAP inclusion

Substance Name (Public Name):	2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol
Chemical Group:	---
EC Number:	204-279-1
CAS Number:	118-82-1
Submitted by:	Umweltbundesamt GmbH on behalf of the Austrian Competent Authority (Austria Federal Ministry of Agriculture, Forestry, Environment and Water Management)
Published:	26/03/2014

Note

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

Contents

1 IDENTITY OF THE SUBSTANCE

1.1 Other identifiers of the substance

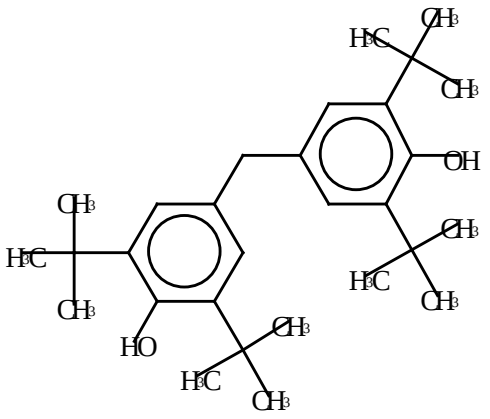
Table 1: Substance identity

EC name:	2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol
IUPAC name:	4,4'-methylenebis(2,6-di-tert-butylphenol)
Index number in Annex VI of the CLP Regulation	---
Molecular formula:	$C_{29}H_{44}O_2$
Molecular weight or molecular weight range:	424,67
Synonyms/Trade names:	4,4'-Methylenebis[2,6-bis(1,1-dimethylethyl)phenol] 4,4'-Methylenebis(2,6-di-tert.-butyl-phenol) 4,4'-Dihydroxy-3,3',5,5'-tetra-tert.-butyl-diphenylmethan 4,4'-Methylenebis(2,6-di-tert.butylphenol) Ethanox 702 and Ionox WTE TBMD (common abbreviation)

In the following the substance 2,2',6,6'-Tetra-*tert*-butyl-4,4'-methylenediphenol is abbreviated with TBMD.

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

Structural formula:



1.2 Similar substances/grouping possibilities

None identified

2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

TBMD is not harmonised classified and therefore not listed in Table 3.1 of Annex VI of the CLP regulation.

2.2 Self classification

- In the registration

  No self-classification has been carried out.

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

Table 2: Additional notified classification and labelling according to CLP criteria (beside of harmonized classification)

Classification		Labelling			Spec. Conc. Limits, M-factors	Notes
Hazard Class and Category Code(s)	Hazard statement code(s)	Pictogram, Signal Word Code(s)	Hazard statement code(s)	Suppl. Hazard statement code(s)		
Aquatic Chronic 2	H411	GHS09	H411	--	--	--
Aquatic Chronic 4	H413		H413	--	--	--
Skin Irrit. 2	H315	GHS07	H315	--	--	--
Eye Irrit. 2	H319	Wng	H319	--	--	--
STOT SE 3	H335		H335	--	--	--
Acute Tox. 4	H312		H312	--	--	--

2.3 Proposal for Harmonised Classification in Annex VI of the CLP

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3 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

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

The substance is used for lubricants and greases covering hydraulic fluids, lubricants, greases, release products and metal working fluids. The intended use covers industrial, professional as well as consumer use. The substance is used i.a. as an antioxidant.

4 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

4.1 Legal basis for the proposal

☐ Article 44(2) (refined prioritisation criteria for substance evaluation)

☒ Article 45(5) (Member State priority)

4.2 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

4.3 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[1]	
☐ 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)

Potential endocrine disruptor

TBMD is structurally similar to Bisphenol A (EC 201-245-8 (CoRAP 2012_DE)) and Bisphenol M (EC 428-970-4 (CoRAP 2014_BE)). The harmonized classification of Bisphenol A according to Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation) is Skin Sens. 1, Eye Dam. 1, STOT SE 3 and Repr. 2. The harmonized classification of Bisphenol M is Skin Sens. 1, Repr. 2 and Aquatic chronic 2. In addition, TBMD is listed within the Endocrine Disruptor Screening Program, Universe of Chemicals for Potential Endocrine Disruptor Screening and Testing (US-EPA)[2] and as Bisphenol A analogs and derivate by NTP[3].
In addition new studies are available.

A new study “Reproduction/Developmental Toxicity Screening Test (2012, in Japanese) is available http://dra4.nihs.go.jp/mhlw_data/jsp/ListPageResultENG.jsp and US-EPA requested a Reproduction/Developmental Toxicity Screening Test with a sun set date 15. May 2012. Both studies have not been included in the CSR. Since spring 2013, the CSA includes a new chronic daphnia study.

Human health concerns (suspected CMR, suspected sensitisiser)

Referring to the registration dossiers, the registrants did not classify TBMD. Based on the classification of the structurally similar substances Bisphenol A (EC 201-245-8) and Bisphenol M (EC 428-970-4 , similar human hazards are considered to be conceivable for TBMD. Therefore, it needs to be assessed, if the current classification of the registrants is correct (e.g. for sensitization).

[1] 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

[2] http://www.epa.gov/endo/pubs/edsp_chemical_universe_list_11_12.pdf

[3] http://ntp.niehs.nih.gov/ntp/htdocs/Chem_Background/ExSumPdf/BisphenolAF_093008_508.pdf

Japanese studies not included in the CSR (2013) are available concerning repeated dose toxicity and mutagenicity (Repeated Dose 28-day Oral Toxicity Study (in Japanese), Bacterial Reverse Mutation Test (in Japanese), In Vitro Mammalian Chromosome Aberration Test (in Japanese). In addition, US-EPA requested new studies for TBMD, which were requested 2006 and 2011 and which should be available since 2012 (sun set date). (http://www.epa.gov/opptintr/chemtest/pubs/sunsettable.html. These studies include mutagenicity. The outcome of the studies is yet unknown.

Suspected PBT/vBvB; Exposure/risk based concerns:

The substance is potentially PBT and potentially hazardous for human health (see chapter 4.5). It is used wide dispersively in hydraulic fluids, lubricants, greases, release products and metal working fluids industrially, professionally and by consumers. No exposure assessment and estimation of release to the environment and exposure of man was 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. If the substance is proven to be PBT or hazardous for human health, an exposure assessment is required for assessing the potential risk for human health and environment and determining, if the given uses can be expected to be safe.

Other hazard based concerns:

Further information on 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.

The Long Range transport potential (LRTP) has been evaluated by Austria and cannot be ruled out (OECD Screening tool).

4.4 Other completed/ongoing regulatory processes that may affect suitability for substance evaluation

☐ Compliance check, Final decision	☐ Dangerous substances Directive 67/548/EEC
☐ Testing proposal	☒ Existing Substances Regulation 793/93/EEC
☐ Annex VI (CLP)	☐ Plant Protection Products Regulation 91/414/EEC
☐ Annex XV (SVHC)	☐ Biocidal Products Directive 98/8/EEC ; Biocidal Product Regulation (Regulation (EU) 528/2012)
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	

The substance is on the list of existing substances that was subject to transitional measures, that is for which there were pending information requests before REACH came into force.

The pending information was received and the evaluation is concluded, see section 4.5.

4.5 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)

Potential endocrine disruptor, Human health concerns, Other hazard based concerns

Potential endocrine disruption and human health hazards are considered to be possible due to the structural similarity of TBMD to Bisphenol A (EC 201-245-8) and Bisphenol M (EC 428-970-4). Referring to the classification given in the registration dossiers, no hazards requiring classification are identified. Furthermore, the substance is not considered to be PBT/vPvB and the ED-concern is not targeted by the registrants. Nevertheless, indications for these potential effects are found in various sources (see description above). Available data for these potential effects and studies used by the registrants need to be assessed. Based on the available data, it will be evaluated, if data requests are considered to be required for clarification of concerns.

Exposure / risk based concerns

If the substance is proven to be PBT or hazardous for human health, an exposure assessment is required for assessing the potential risk for human health and environment and determining, if the given uses can be expected to be safe.

Suspected PBT / vBvB

2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol (TBMD) was discussed by the TCNES PBT Working Group. As a result of these discussions industry carried out a fish bioaccumulation study (OECD TG 305), which was requested for TBMD under Commission Regulation (EC) No. 465/2008 (Bioconcentration study on fish (OECD 305 or dietary study) within 18 months). This study has now been completed and is summarised in the factsheet prepared by the PBT Working Group (Blankinship et al. 2009 and 2010[1]; ECHA, 2014).

In the bioconcentration study of Blankinship et al. (2009, 2010), the growth rate constant (0.017 day^{-1}, Environmental Risk Evaluation Report: TBMD) is close to the overall depuration rate constant (0.020 day^{-1}) indicating that growth dilution is the main “depuration” process. Due to the significant fish growth (from 5.88 g to around 16 g), the kinetic BCF corrected for growth is preferred over the steady-state BCF. The growth-corrected and lipid-standardized BCF value is around 14,100 l/kg (EA, 2011; in preparation) based on C^{14}-analysis. Approximately 60% of the ^{14}C in fish at steady-state is parent compound; this would imply a revised BCF for the parent substance of TBMD of 8,640 L/kg (lipid- and growth-corrected) (EA, 2011; in prepartion). In another study, the measured steady state BCF values from the NITE website (4,600 – 9,200 l/kg) indicate a high bioaccumulation potential. A dietary study yielded a BMF value of 0.95, which is higher than the BMF for hexachlorbenzol used within the same study. The BCF may be derived from the dietary data resulting in BCF values > than 5,000.

At the current state, it is concluded, that the BCF value of **TBMD is ≥ 5,000 L/kg**, so the substance **meets** the **bioaccumulative (B)** and the **very bioaccumulative (vB) criterion** according to Annex XIII of REACH.

[1] The study report Blankinship et al. 2009 was amended 2010 with modified calculations for lipid content, estimation of t_{90}, $t_{1/2}$, k_1 and k_2.

Based on the BIOWIN-predictions, TBMD is expected to be persistent in the environment. A former study on ready biodegradability showed no degradation of the substance within 28 days as evidenced by CO2 formation. However, it was noted that the concentration used was far above the water solubility. The substance undergoes rapid primary degradation; however several major potential persistent metabolites arise, but their identities remain unknown. Therefore more information regarding the identity and the degradation pathway of the degradation products is necessary. This is also outlined in the REACH Guidance on information requirements and chemical safety assessment Chapter R.7c: Endpoint specific guidance (ECHA; 2008b): When a substance is not fully mineralised, but degraded to more persistent degradation products, the PBT/vPvB properties of these should be evaluated before a final judgment of whether a substance fulfils the persistence criteria can be drawn. No simulation tests based on TG OECD 307, 308, or 309 are available.

Regarding ecotoxicity, only limited data are available and the presented data mostly refers to acute toxicity which is of limited reliability. According to information given in the registration dossier a long term test on invertebrates has been conducted, but a long-term toxicity study on fish (Annex IX, section 9.1.6.) was incorrectly waived. According to column 2 of Annex VII 9.1.1. and of Annex VIII section 9.1.3., long-term toxicity testing shall be considered for substances that are poorly water soluble. The given adaptation is therefore unacceptable. Based on the available data currently no conclusion on the T criterion is possible.

Conclusion

During the substance evaluation process it has to be clarified if the P and/or T criterion is met for TBMD. Therefore, an indepth assessment of the presented and/or outstanding data has to be carried out. If the substance is PBT or vPvB, an exposure assessment is required for estimating the risk of the given uses.

References:

Blankinship, A.; Kendall, T.Z.; Krueger, H.O. (2009). 2,2',6,6'-TETRA-T-BUTYL-4,4-METHYL DIPHENOL: A bioconcentration test with the rainbow trout (Oncorhynchus mykiss), Report. Wildlife International, Ltd, Project Number: 471A-114.

Blankinship, A.; Kendall, T.Z.; Krueger, H.O., (2010). 2,2',6,6'-TETRA-T-BUTYL-4,4-METHYL DIPHENOL: A bioconcentration test with the rainbow trout (Oncorhynchus mykiss), Amended Report. Wildlife International, Ltd, Project Number: 471A-114.

EA, 2011: Environment Agency of England & Wales: Estimation of fish bioconcentration factor (BCF) from depuration data. Science Report SCHO0811BUCE-E-E.

ECHA, 2014; PBT Working group; Summary factsheet. Results of evalution of the PBT/vPvB properties of 2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol.
http://echa.europa.eu/documents/-10162/13628/tetra_tertrtbutyl_pbtsheet_en.pdf

4.6 Potential follow-up and link to risk management

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