Justification for the selection of a candidate CoRAP substance

Substance Name (Public Name):	di-tert-butyl peroxide
Chemical Group:	Peroxides
EC Number:	203-733-6
CAS Number:	110-05-4
Submitted by:	RIVM, the Netherlands
Published:	20/03/2013

NOTE

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

Contents

1 IDENTITY OF THE SUBSTANCE

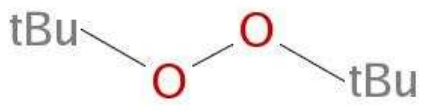
1.1 Name and other identifiers of the substance

Table 1: Substance identity

Public Name:	di-tert-butyl peroxide
EC number:	203-733-6
EC name:	di-tert-butyl peroxide
CAS number (in the EC inventory):	110-05-4
CAS number:	110-05-4
CAS name:	Peroxide, bis(1,1-dimethylethyl)
IUPAC name:	2,2'-dioxybis(2-methylpropane)
Index number in Annex VI of the CLP Regulation	617-001-00-2
Molecular formula:	C8H18O2
Molecular weight or molecular weight range:	146.2273
Synonyms:	Peroxide, bis(1,1-dimethylethyl) tert-Butyl peroxide dTBP

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

Structural formula:



2 CLASSIFICATION AND LABELLING

2.1 Harmonised Classification in Annex VI of the CLP

Flam. Liquid 2, H225: Highly flammable liquid and vapour.

Org. Perox. Type E, H242: Heating may cause a fire.

Muta. 2; H341: Suspected of causing genetic defects (3rd ATP to CLP; Commission Regulation (EU) No 618/2012).

DSD criteria table 3.2:

O; R7 Oxidising; May cause fire.

F; R11 Highly flammable; Highly flammable

Muta. Cat. 3;R68: Possible risk of irreversible effects. (3rd ATP to CLP; Commission Regulation (EU) No 618/2012).

2.2 Proposal for Harmonised Classification in Annex VI of the CLP

Not relevant

2.3 Self classification

CLP criteria:

Classification by the lead registrant is consistent with harmonised classification and additionally includes the following classification:

Aquatic Chronic 3; H412: Harmful to aquatic life with long lasting effects.

DSD criteria:

Classification by the lead registrant is consistent with harmonised classification according to DSD criteria table 3.2 and additionally includes the following classification;

R52/53 - harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

C&L additionally includes the following classifications:

Acute Tox. 4; H332: Harmful if inhaled.

3 JUSTIFICATION FOR THE SELECTION OF THE CANDIDATE CoRAP SUBSTANCE

3.1 Legal basis for the proposal

☐ Article 44(1) (refined prioritisation criteria for substance evaluation)

☒ Article 45(5) (Member State priority)

3.2 Grounds for concern

☒ (Suspected) CMR	☒ Wide dispersive use	☐ Cumulative exposure
☐ (Suspected) Sensitiser	☒ Consumer use	☐ High RCR
☐ (Suspected) PBT	☐ Exposure of sensitive populations	☒ Aggregated tonnage
☐ Suspected endocrine disruptor	☐ Other (provide further details below)	

Suspected CMR

- Mutagenicity
  - Three *in vitro* studies (two Ames tests and one mouse lymphoma assay) were negative and one Ames test was considered invalid.
  - One *in vivo* spermatogonial chromosome aberration test was negative according to the registrant. No statistically significant increase in the percentage of aberrant cells and no dose-related decrease of the mitotic index were observed in the test article-treated groups relative to the vehicle control ($p > 0.05$ Fisher's exact test). The individual number of chromosome aberrations (or summary) were not given.
  - One *in vivo* micronucleus test in bone marrow gave a positive result. Di-tert-butyl peroxide induced damage to the chromosomes or the mitotic apparatus of mice bone marrow cells after two intraperitoneal administrations, at a 24-hour interval, at the dose-levels of 500, 1000 and 2000 mg/kg/day. The numbers of micronuclei were not reported.
  - A second *in vivo* micronucleus test was performed and described, but no results were given.
- No carcinogenicity studies were provided. No scientific base was given for not providing the information. Only one repeated dose toxicity study (OECD 422 combined repeated dose toxicity study) was available.
- No effects on the reproductive organs were found in a combined repeated dose and reproduction / developmental screening study.

Based on the provided data, no conclusions can be drawn about the proposed classification for mutagenicity. The results (number of micronuclei, number of chromosome aberrations) of all three *in vivo* studies should be provided to further evaluate the mutagenicity. A germ cell mutagenicity test should be provided to determine if di-tert-butyl peroxide should be classified as Muta 1B. According to the RAC opinion, di-tert-butyl peroxide should be classified as Muta 2 based on the current data. Sufficient data for germ cell mutagenicity and carcinogenicity data are lacking.

Tonnage

The total tonnage level of this substance is over 1000 tonnes.

Exposure

For professional uses and consumers indoor and outdoor use multiple process categories (brushing, spraying, treatment of articles by dipping and pouring, hand-mixing) and product categories (adhesives, sealants, air care products, finger paints, inks, polishes, cosmetics, washing and cleaning products, etc) are described, but no exposure scenarios or estimations were provided for professional use and consumer use. For consumers it is noted by the registrant that consumer exposure is 'not applicable as consumers are not involved in manufacture and in the industrial use of preparations containing the substance. Furthermore, a release of the substance from the final product is not expected. Exposure of consumers to the substance during handling of articles can be ruled out'. The risk for professional use and consumers use can therefore not be characterized. The exposure assessment tool ART was used applying a vapour pressure of 10 Pa whereas the determined vapour pressure was 3500 Pa. This may result in an incorrect exposure estimate. Overall, the concern on consumer exposure of dispersive use cannot be removed at this stage.

3.3 Information on aggregated tonnage and uses

☐ 1 – 10 tpa	☐ 10 – 100 tpa	☐ 100 – 1000 tpa
☐ 1000 – 10,000 tpa	☐ 10,000 – 100,000 tpa	
☒ 1000 + tpa	☐ 100,000 – 1000,000 tpa	☐ > 1000,000 tpa
☒ Confidential		
Some tonnage is claimed confidential.		

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

Manufacture, formulation and industrial use of organic peroxides as polymerization initiators, crosslinking agents or curing agents were listed. Consumer indoor use of organic peroxides in non-polymer applications includes adhesives, sealants, air care products, biocidal products (e.g. disinfectants, pest control), coatings and paints, thinners, paint removes, modelling clay, finger paints, ink and toners, polishes and wax blends, washing and cleaning products (including solvent based products), cosmetics, personal care products.

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

☐ Compliance check	☐ 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
☐ Annex XIV (Authorisation)	☐ Other (provide further details below)
☐ Annex XVII (Restriction)	

There is testing proposal with the following end points: 4.22 Viscosity (TP end point 1), 5.2.2 Biodegr. in water and sediment (TP endpoint 2), 6.1.2 Long-term tox. fish (TP endpoint 3), 6.1.4 Long-term tox. aquatic invert (TP endpoint 4), 7.5.1 Repeated tox. oral (TP endpoint 5), and 7.8.2 Develop. Tox. / teratogen (TP endpoint 6). The final decision sent on 02/08/2012 and the dossier is expected to be updated until 02/08/2014.

3.5 Information to be requested to clarify the suspected risk

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

Information on toxicological properties:
Repeated dose toxicity: OECD Guideline 408 (Repeated Dose 90-Day Oral Toxicity in Rodents)
Developmental toxicity: OECD 414 developmental toxicity study.
A carcinogenicity and a germ cell mutagenicity study are foreseen to be requested.

Exposure

For professional and consumer indoor and outdoor use multiple process categories (brushing, spraying, treatment of articles by dipping and pouring, hand-mixing) and product categories (adhesives, sealants, air care products, finger paints, inks, polishes, cosmetics, washing and cleaning products, etc) are described, but no exposure scenarios or estimations were provided for professional use and consumer use. The risk for professional use and consumers use can therefore not be characterized.

3.6 Potential follow-up and link to risk management

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

Non-conclusive at this stage.