



**Ministry of Environment  
and Food of Denmark**  
Environmental  
Protection Agency

## **Justification Document for the Selection of a CoRAP Substance**

**Substance Name (public name):** 2,2-Dimethylpropan-1-ol, tribromo  
derivative

**EC Number:** 253-057-0

**CAS Number:** 36483-57-5

**Authority:** Danish Environmental Protection  
Agency

**Date:** 21/03/2017

### **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

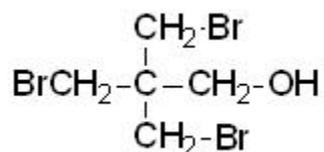
### 1.1 Other identifiers of the substance

**Table: Other Substance identifiers**

<b>EC name (public):</b>	2,2-Dimethylpropan-1-ol, tribromo derivative
<b>IUPAC name (public):</b>	3,3,3-tribromo-2,2-dimethylpropan-1-ol
<b>Index number in Annex VI of the CLP Regulation:</b>	-
<b>Molecular formula:</b>	C <sub>5</sub> H <sub>9</sub> Br <sub>3</sub> O
<b>Molecular weight or molecular weight range:</b>	>324.0 - <325.0
<b>Synonyms:</b>	<i>FR-513 (trade name)</i> <i>TBNPA (abbreviation)</i> <i>Tribromoneopentyl alcohol</i>

**Type of substance**     Mono-constituent     Multi-constituent     UVCB

#### Structural formula:



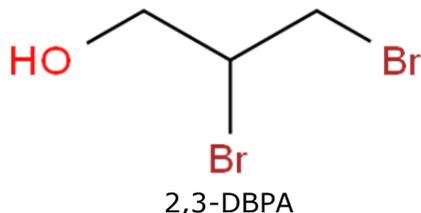
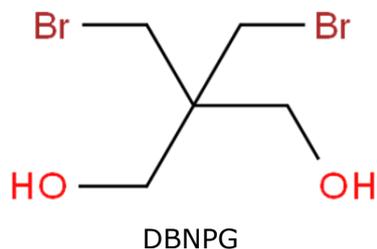
### 1.2 Similar substances/grouping possibilities

Two other similar substances based on a structural similar signature (brominated small alkyl alcohols) may be relevant to explore for a potential grouping approach or read across. This is:

1. The REACH registered substance 2,2-bis(bromomethyl)propane-1,3-diol (DBNPG), CAS no 3296-90-0, which is currently on the PACT list.
2. The pre-registered substance 2,3-Dibromo-1-propanol (2,3-DBPA), CAS no 96-13-9.

A possible grouping approach for these substances is further described in the following publication: Category approach for selected brominated flame retardants (Wedebye et al. 2016) available at: <http://www2.mst.dk/Udgiv/publications/2016/07/978-87-93435-90-2.pdf>

**Structural formula:**



## 2 OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

**Table: Completed or ongoing processes**

RMOA	<input type="checkbox"/> Risk Management Option Analysis (RMOA)	
REACH Processes	Evaluation	<input type="checkbox"/> Compliance check, Final decision
		<input checked="" type="checkbox"/> Testing proposal Testing proposal, Final decision. Prenatal development study (OECD TG 414) on the registered substance, ongoing.
		<input type="checkbox"/> CoRAP and Substance Evaluation
	Authorisation	<input type="checkbox"/> Candidate List
		<input type="checkbox"/> Annex XIV
Restriction	<input type="checkbox"/> Annex XVII <sup>1</sup>	
Harmonised C&L	<input type="checkbox"/> Annex VI (CLP) (see section 3.1)	
s under other EU	<input type="checkbox"/> Plant Protection Products Regulation Regulation (EC) No 1107/2009	

<sup>1</sup> Please specify the relevant entry.

	<input type="checkbox"/> Biocidal Product Regulation Regulation (EU) 528/2012 and amendments
Previous legislation	<input type="checkbox"/> Dangerous substances Directive Directive 67/548/EEC (NONS)
	<input type="checkbox"/> Existing Substances Regulation Regulation 793/93/EEC (RAR/RRS)
(UNEP) Stockholm convention (POPs Protocol)	<input type="checkbox"/> Assessment
	<input type="checkbox"/> In relevant Annex
Other processes / EU legislation	<input type="checkbox"/> Other (provide further details below)
Further details	

### 3 HAZARD INFORMATION (INCLUDING CLASSIFICATION)

#### 3.1 Classification

##### 3.1.1 Harmonised Classification in Annex VI of the CLP

There is no harmonised classification of the substance.

##### 3.1.2 Self classification

- In the registration:  
Eye Irrit. 2 (H319: Causes serious eye irritation)
- The following hazard classes are in addition notified among the aggregated self classifications in the C&L Inventory:
  - There are 69 notifiers self-classifying the following: Aquatic Chronic 3 (H412).
  - There are 24 notifiers self-classifying the following: Eye Irrit. 2 (H319); Aquatic Chronic 3 (H412).
  - There are 15 notifiers self-classifying the following: Acute Tox. 4 (H302); Muta 2 (H341).
  - There are 6 notifiers self-classifying the following: Eye Irrit. 2 (H319); Muta 1B (H340); Carc. 1B (H350).

### 3.1.3 Proposal for Harmonised Classification in Annex VI of the CLP

There are no proposals for Harmonised Classification in Annex VI of the CLP.

## 4 INFORMATION ON (AGGREGATED) TONNAGE AND USES<sup>2</sup>

### 4.1 Tonnage and registration status

**Table: Tonnage and registration status**

<b>From ECHA dissemination site</b>		
<input checked="" type="checkbox"/> Full registration(s) (Art. 10)	<input checked="" type="checkbox"/> Intermediate registration(s) (Art. 17 and/or 18)	
Tonnage band (as per dissemination site)		
<input type="checkbox"/> 1 – 10 tpa	<input type="checkbox"/> 10 – 100 tpa	<input checked="" type="checkbox"/> 100 – 1000 tpa
<input type="checkbox"/> 1000 – 10,000 tpa	<input type="checkbox"/> 10,000 – 100,000 tpa	<input type="checkbox"/> 100,000 – 1,000,000 tpa
<input type="checkbox"/> 1,000,000 – 10,000,000 tpa	<input type="checkbox"/> 10,000,000 – 100,000,000 tpa	<input type="checkbox"/> > 100,000,000 tpa
<input type="checkbox"/> <1 . . . . . >+ tpa (e.g. 10+ ; 100+ ; 10,000+ tpa)		<input type="checkbox"/> Confidential
There are 2 registration dossiers, one full registration in the tonnage band 100-1000 tpa and one intermediate registration for intermediate use only.		

### 4.2 Overview of uses

The substance is used as a reactive flame retardant in polymers synthesis (100-1000 tpa) for the manufacture of plastic products and chemicals. It is used in industrial, professional and consumer settings in formulation and use of commercial mixture(s).

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<sup>2</sup> Information compiled in May 2016.

**Table: Uses**

**Part 1:**

<input type="checkbox"/> Manufacture	<input checked="" type="checkbox"/> Formulation	<input checked="" type="checkbox"/> Industrial use	<input checked="" type="checkbox"/> Professional use	<input checked="" type="checkbox"/> Consumer use	<input type="checkbox"/> Article service life	<input checked="" type="checkbox"/> Closed system
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**Part 2:**

	<b>Use(s)</b>
<b>Uses as intermediate</b>	Use in closed batch process (synthesis or formulation) PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing).  SU 8: Manufacture of bulk, large scale chemicals (including petroleum products). SU 9: Manufacture of fine chemicals
<b>Formulation</b>	Tribromoneopentyl alcohol is used in formulation of mixtures and polymers. Tribromoneopentyl alcohol is used in batch and other process (synthesis) where opportunity for exposure arises including including mixing or blending for formulation of preparations and articles (multistage and/or significant contact).
<b>Uses at industrial sites</b>	Uses include PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact), PROC 7: Industrial spraying, PROC 10: Roller application or brushing, PROC 13: Treatment of articles by dipping and pouring, PROC 14: Production of preparations or articles by tableting, compression, extrusion, palletisation, PROC 15: Use as laboratory reagent, PROC 21: Low energy manipulation of substances bound in materials and/or articles.
<b>Uses by professional workers</b>	Uses include wide dispersive indoor and outdoor use of reactive substances in open systems. PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities, PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities, PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact), PROC 10: Roller application or brushing, PROC 11: Non industrial spraying, PROC 13: Treatment of articles by dipping and pouring, PROC 21: Low energy manipulation of substances bound in materials and/or articles.
<b>Consumer Uses</b>	Wide dispertive indoor and outdoor use of reactive substances in open systems. PC 32: Polymer preparations and compunds.
<b>Article service life</b>	

## 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 <input type="checkbox"/> C <input type="checkbox"/> M <input type="checkbox"/> R	Suspected CMR <sup>1</sup> <input checked="" type="checkbox"/> C <input checked="" type="checkbox"/> M <input type="checkbox"/> R	<input type="checkbox"/> Potential endocrine disruptor
<input type="checkbox"/> Sensitiser	<input type="checkbox"/> Suspected Sensitiser <sup>3</sup>	
<input type="checkbox"/> PBT/vPvB	<input type="checkbox"/> Suspected PBT/vPvB <sup>1</sup>	<input type="checkbox"/> Other (please specify below)
Exposure/risk based concerns		
<input type="checkbox"/> Wide dispersive use	<input type="checkbox"/> Consumer use	<input type="checkbox"/> Exposure of sensitive populations
<input type="checkbox"/> Exposure of environment	<input type="checkbox"/> Exposure of workers	<input type="checkbox"/> Cumulative exposure
<input type="checkbox"/> High RCR	<input type="checkbox"/> High (aggregated) tonnage	<input type="checkbox"/> Other (please specify below)

<sup>3</sup> 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

In the 30-day study, kidney and urinary bladder were identified as target organs with renal tubular damage observed in the kidney and generalized hyperplasia in the urinary bladder.

TBNPA showed no evidence of mutagenic activity in the absence or presence of rat liver S9, but showed a clear evidence of mutagenic activity in strains TA100 and TA1535 in the presence of hamster liver S9. It also gave positive results in the mouse lymphoma assay in the presence of rat liver S9. Increases in chromosomal aberrations were induced in cultured peripheral human lymphocytes in the presence of metabolic activation, and at the highest test substance concentration in the absence of metabolic activation. The substance did not induce any marked or significant increases in the incidence of cells undergoing unscheduled DNA synthesis in isolated rat liver cells following *in vivo* exposure and therefore, the substance was considered to be non-genotoxic in this study. Furthermore, the substance did not increase the frequency of micronucleated polychromatic erythrocytes in the bone marrow in mice. (Study reports, cited from the REACH Registration Dossier Database).

Overall, TBNPA showed mutagenic/genotoxic activity *in vitro* in the presence of a metabolic activation system. However, the only relevant follow up *in vivo* study for gene mutation – the UDS study – is known to have limitations, and hence it can neither be concluded or excluded if TBNPA is an *in vivo* mutagen.

Based on the findings for the two structural analogous substances in the 2-year NTP studies with 2,3-DBPA (NTP 1993) and DBNPG (NTP 1996), as well as the discussion on the underlying mode/mechanisms of action for the carcinogenic effect of these two brominated flame retardants provided in the NTP reports (NTP 1996, 1993), and harmonised/notified classification(s), the critical effect of these two brominated flame retardants is the multiple-organ carcinogenic effect, most probably exerted by a genotoxic mode of action either by the parent compound itself (2,3-DBPA) or by a metabolite of the parent compound (DBNPG).

Whether TBNPA also has carcinogenic properties cannot be concluded based on the available data.

TBNPA has a notified classification: Muta. 1B H340 / Muta. 2 H341; Carc. 1B H350.

In conclusion, there is a concern that TBNPA could be a genotoxic carcinogen most probably linked to a genotoxic metabolite of the parent compound, as the *in vitro* mutagenic/genotoxic responses were shown to require the presence of metabolic activation. A substance evaluation is needed in order to clarify this identified concern.

A combination of the suspected toxicological effects, high tonnage use in combination with a high potential for worker exposures (e.g. PROC 7(industrial), 10 (industrial and professional) and 11(professional)) and consumer exposures (wide dispersive indoor and outdoor uses of the reactive substance in open systems adds up to the overall concerns contributing to why it is selected for CoRAP inclusion.

**5.4. Preliminary indication of information that may need to be requested to clarify the concern**

<input checked="" type="checkbox"/> Information on toxicological properties	<input type="checkbox"/> Information on physico-chemical properties
<input type="checkbox"/> Information on fate and behaviour	<input type="checkbox"/> Information on exposure

<input type="checkbox"/> Information on ecotoxicological properties	<input type="checkbox"/> Information on uses
<input type="checkbox"/> Information ED potential	<input checked="" type="checkbox"/> Other (provide further details below)
Depending on the results of the evaluation further studies may be needed to clarify the concerns for mutagenicity and/or carcinogenicity. This may also involve requests for further information on toxicokinetics, including metabolism.	

**5.5. Potential follow-up and link to risk management**

<input checked="" type="checkbox"/> Harmonised C&L	<input checked="" type="checkbox"/> Restriction	<input checked="" type="checkbox"/> Authorisation	<input type="checkbox"/> Other (provide further details)
Further information on concern for mutagenicity and carcinogenicity may lead to proposal for harmonized C&L and possibly nomination for the Candidate List. A restriction proposal could also be relevant.			