



**Ministry of Environment  
and Food of Denmark**

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Protection Agency

# Pre-screening of REACH registration dossiers for 9 brominated flame retardants

- A LOUS follow-up project

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**Title:**

Pre-screening of REACH registration dossiers for  
9 Brominated flame retardants

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# Preface

The use of brominated flame retardants (BFRs) in consumer products with known human exposure are in focus nationally and internationally due to possible human and environmental effects. The effects in focus are possible human reproductive and endocrine disrupting effects and biopersistsens, accumulation and toxicity in the environment (PBT).

The overall purpose of this project was to make an overview on the toxicological and ecotoxicological effects as presented in the REACH-registrations of 9 selected BFRs identified by the Danish Environmental protection Agency (Danish EPA). This was based on the public available data, retrieved from the disseminated registration dossiers under REACH submitted by the industry.

The outcome of the project is a table of the 9 BFRs each described by a data sheet with key information on the toxicological and ecotoxicological profiles. If concern is concluded based on the available data sets, recommendation for further substance evaluation has been be concluded and relevant justification documents filled in.

This project was carried out during the period from September 2014 to December 2014.

The project was implemented by DHI by a project team consisting of Brian Svend Nielsen (project manager), Tina Slothuus and Poul Bo Larsen (Quality supervisor and assurance).

The project was advised by a steering committee consisting of  
Jesper Gruvmark, the Danish EPA  
Mikkel Aamann, the Danish EPA  
Brian Svend Nielsen, DHI  
Poul Bo Larsen, DHI.

# Summary and conclusions

A toxicological and ecotoxicological pre-screening of 9 selected (BFRs) were performed using data extracted from the latest REACH disseminated registration dossiers on the ECHA homepage. Data were extracted from October to November 2014. Evaluations of the 9 BFRs have been based on the study summaries and conclusions drawn in the disseminated registration dossiers on the ECHA homepage. For each endpoint, key studies, supplementary studies and weight of evidence studies (if needed) from the registration are described.

It is emphasised that all conclusions drawn in the registration dossiers are the responsibility of the registrants, and that all information in terms of no-effect level setting, DNELs/PNECs and the use of read-across have been referred to without further evaluation.

For each of the 9 BFRs, registration data with identification of the substance, important physical-chemical characteristics and the toxicological and ecotoxicological data are included in a data sheet for each of the 9 BFR substances (Annex 1). For each endpoint, key studies, supplementary studies and weight of evidence studies (if evaluated to be needed) from the registration are described.

Based on the registration data in Annex 1, conclusions on the most important endpoints have been drawn and are summarised in Table 2 and 3 below describing the key toxicological and ecotoxicological properties (the lowest NOAEL and critical effect is indicated). Also, an evaluation of the available data sets in terms of quality and completeness is included in Table 4.

With regard to priority for further evaluation the following conclusions were drawn for the BFRs, using the below described criteria for prioritisation. (High tonnage levels indicating a higher potential for exposure may further add to concern).

*Low level priority:* although data gaps occur, the available data do not indicate specific concern for some of the critical endpoints (CMR and PBT or endocrine disruption).

*Medium Level:* large data gaps are identified for hazard evaluation of critical endpoints (CMR and PBT or endocrine disruption), and the preliminary evaluation of concern is non-conclusive.

*High level:* available data indicate concern for some of the critical endpoints (CMR and PBT or endocrine disruption) and further evaluation is needed (and/or testing is needed in order to clarify the indicated concern).

The BFRs indicated with the highest priority may be recommended for further substance evaluation. For these substances justification documents (“Justification document for the selection of a CoRAP<sup>1</sup> substance”) for suggested further substance evaluation will be filled out.

As indicated below a total of 3 BFRs was prioritized for further substance evaluation: HEEHP-TEBP (CAS: 20566-35-2), BEH-TEBP (BEHTBP) (CAS: 26040-51-7) and DBNPG (CAS: 3296-90-0).

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<sup>1</sup> Community rolling action plan

Short conclusions on the pre-screened BFRs:

**TBP (2,4,6-TBP) (CAS: 118-79-6):** The substance is already on the CoRAP-list as suspect CMR and PBT properties. Thus at this moment the substance is already considered a candidate of substance evaluation. Large data gaps are identified. Further, the registrant concludes that the substance is not a PBT substance. However, due to lack of data, P cannot be assessed based on the PBT criteria. TBP does not fulfil the screening criteria for B and T. A tonnage band up to 10000 tonnes/y is indicated.

Conclusion: *Low priority as the substance is already on CoRAP-list.*

**TTBNPP (19186-97-1):** Data are lacking on carcinogenicity, and mutagenicity is not fully examined. The available data on reproductive and developmental toxicity do not indicate any specific concern, however no two-generation reproduction study is available (or alternatively an extended one-generation reproduction study). The registrant concludes that the substance is not a PBT substance. However, in relation to PBT criteria, TBNPP does fulfil the screening criteria for P (not readily biodegradable) but not the criteria for B and T. The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *Low priority.*

**HEEHP-TEBP (CAS: 20566-35-2):** Very few data are available on the substance. Read-across is used in the registration dossier. Data on reproductive and developmental toxicity are lacking. The data set is very slim and the read-across should be further evaluated. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT, HEEHP-TEBP does not fulfil the screening criteria for P (however only QSAR), B (only calculated value) and T. Based on the structural resemblance to DEHP and the lack of data on reproductive and developmental toxicity, a need for further evaluation is indicated. The tonnage band is indicated to be up to 100 tonnes/y.

Conclusion: *High priority.*

**TTBP-TAZ (CAS: 25713-60-4):** Data on CMR properties is limited, however a two-generation reproduction study and a developmental toxicity study are proposed by the registrant. A 90D study does not give reason to specific alert for carcinogenicity and reproductive toxicity. The registrant concludes that the substance is not a PBT substance. However, it is not readily biodegradable (screening criteria for P, vP fulfilled) and QSAR calculations indicate a potential for bioaccumulation (Log Kow > 4.5). Therefore, B and vB potential needs to be further evaluated. An RMOA is being performed at the moment based on *suspected* PBT properties. The tonnage band is indicated to be up to 10000 tonnes/y. The registration does not fulfil the data requirements for an Annex X registration but testing is proposed by registrant.

Conclusion: *Low priority based on an ongoing RMOA.*

**BEH-TEBP (BEHTBP) (CAS: 26040-51-7):** Large data gaps in the registration, Data on CMR properties are limited. Some alert (mutagenicity) could be raised from the available from in vitro testing. A developmental toxicity study is proposed by the registrant. A concern could be raised due to the structural resemblance with DEHP. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT screening criteria, BEH-TEBP does fulfil the screening criteria for P but not B and T. Data on accumulation in biota does, however, indicate a bioaccumulation potential. The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *high priority*

**EBTEBPI (CAS: 32588-76-4):** Data on CMR properties are limited, however there is no indication of concern in the available data on developmental and repeated dose toxicity (90d). The registrant concludes that the substance is not a PBT. However, in relation to PBT screening criteria, EBTEBPI does fulfil the screening criteria for P (not ready biodegradable) but not B and T. The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *Low priority*

**DBNPG (CAS: 3296-90-0):** The available data on CMR endpoints indicate a concern for carcinogenic and mutagenic effects as well as possible toxicity to reproduction. Data are available from *in vitro* and *in vivo* studies showing that DBNPG is genotoxic with multi-site carcinogenic activity. Registrant has (only) classified as Carc. 2..

The registrant concludes that the substance is not a PBT substance. However, in relation to PBT criteria, DBNPG does fulfil the screening criteria for P (not ready biodegradable and inherently biodegradability is < 70%) and T (maybe fulfilled if classified as Carc. 1b.) but not B.

The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *high priority*

**TEBP-Anh (CAS: 632-79-1):** Very few data are available on the substance and read-across is used widely in the registration dossier. In general, data are lacking on reproductive and developmental toxicity. A concern for organ toxicity is noted from a repeated dose toxicity study. The data set is sparse and the justification for the applied read-across should be further evaluated. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT screening criteria, TEBP-Anh does fulfil the screening criteria for P (not ready biodegradable) but not B and T.

The tonnage band is indicated to be up to 100 tonnes.

Conclusion: *Medium*

**2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS: 68441-62-3):** Data on CMR properties are limited and there are some indications on mutagenic activity based on *in vitro* assays, however *in vivo* data are negative. The registrant proposes to carry out a two-generation reproduction study and a developmental toxicity study. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT screening criteria, 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated does fulfil the screening criteria for P (not ready biodegradable) but not B and T. The tonnage band is indicated to be up to 10 000 tonnes. The substance should be re-evaluated when testing has been performed.

Conclusion: *Low/medium priority*

It should be noted that for none of the substances there were data or discussion of possible endocrine disrupting properties or on combination effects with similar substances. However, indicative findings on 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS 68441-62-3) suggests effects on sperm morphology. It is noted that the data were from a short-term repeated dose toxicity study.

*Overall conclusion:*

TBP (2,4,6-TBP) (CAS: 118-79-6) and TTBP-TAZ (CAS: 25713-60-4) are given low level prioritization due to on-going REACH activities (RMOA and CoRAP-list).

TTBNPP (19186-97-1) and EBTEBPI (CAS: 32588-76-4) are given low level prioritization due to no serious alert from existing data. Data gaps identified.

2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS: 68441-62-3) is given low/medium level prioritization due to on-going REACH activities (testing proposed by registrant).

TEBP-Anh (CAS: 632-79-1) is given medium prioritization due to data-gaps (reproductive and developmental toxicity), a concern for organ toxicity and the use of read-across. However, very low tonnage.

*And based on the current evaluation, HEEHP-TEBP (CAS: 20566-35-2), BEH-TEBP (BEHTBP) (CAS: 26040-51-7) and DBNPG (CAS: 3296-90-0) are given high level prioritization and recommended for further evaluation.*



# 1. Introduction

In general, flame retardants are added to polymeric materials, both natural and synthetic, to enhance the flame-retardant properties of the polymers. Brominated flame retardants (BFRs) have in common that they contain bromine and are used to prevent the ignition of plastic materials and textiles. They all act by the same mechanism: through the release of hydrogen bromine when the material is ignited which interrupts the further combustion process. Otherwise, the brominated flame retardants form a complex group of substances, i.e. aromatic, cycloaliphatic, aliphatic, polymeric and inorganic substances, all containing bromine.

Some of the substances are used as additives, where the substances are not chemically bound in the polymer material, while others are used as reactive substances that chemically bound in the polymer structure and not present as the original substance in the final polymer (except for trace amounts of un-reacted substances)<sup>2</sup>.

In a recent survey of BFRs by the Danish EPA<sup>2</sup>, a large number of BFRs were identified and examined, including 69 BFRs which have been preregistered under REACH and/or are produced by the major international manufacturers of brominated flame retardants. Furthermore, 14 substances described in the literature, but not preregistered or marketed by the major manufactures, were examined in this survey. The main objective with this survey was to provide background for the Danish EPA's consideration regarding the need for further risk management measures.

In connection to this survey, the Danish EPA has established a list of 9 BFRs which need further examination in relation to toxicological and ecotoxicological properties based on recent REACH registrations. The outcome of this project will be an overview of the available data for each of the 9 BFRs, including an identification of data-gaps in relation to a full toxicological/ecotoxicological profile. The data-gap analysis compared available data in the REACH registration dossiers to the data requirements for a high tonnage registration (> 1000 tpa, Annex X). Special attention was paid to reproductive toxicity and possible endocrine disrupting effects and PBT assessment.

Based on the overview of data and the data-gap analyses the 9 BFRs are prioritised for further need for e.g. a substances evaluation (inclusion on the CoRAP-list) or other regulatory action.

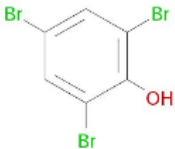
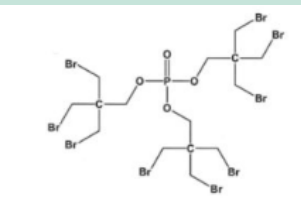
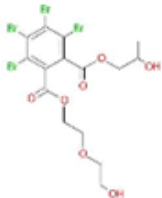
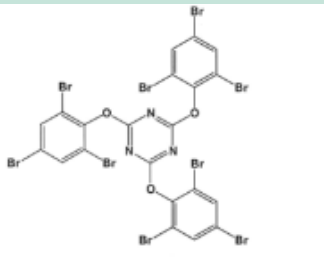
The 9 BFRs are identified below in Table 1 (substance name, abbreviation, CAS No) together with the harmonised and notified classifications and the tonnage band for the REACH registrations. For each of the 9 BFRs, a dossier data set with identification of the substance, important physical-chemical characteristics and the toxicological and ecotoxicological data is included in a data sheet (Annex 1). For each endpoint, key studies, supplementary studies and weight of evidence studies (if needed when data from key studies were not sufficient to draw conclusions) from the registration are described.

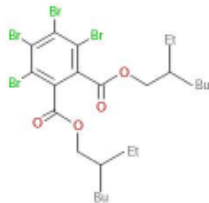
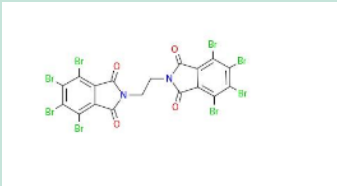
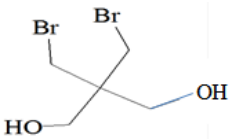
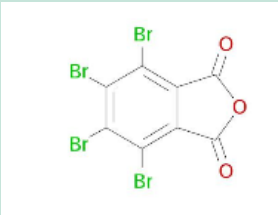
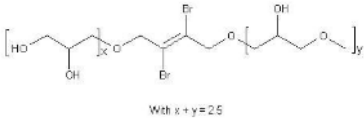
Based on the data sets in Annex 1, conclusions on the most important endpoints have been drawn and summarised in Tables 2 and 3 below describing the key toxicological and ecotoxicological properties (the lowest NOAEL and critical effect is indicated). Also, an evaluation of the available data sets in terms of quality and completeness is included in Table 4.

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<sup>2</sup> Danish EPA, survey of brominated flame retardants, part of the LOUS-review, Environmental Project No. 1536, 2014.

**TABLE 1**  
 OVERVIEW OF THE 9 BROMINATED FLAME RETARDANTS: SUBSTANCE NAME, ABBREVIATION, CAS NO, CHEMICAL STRUCTURE, INDICATIONS ON AVAILABLE CLASSIFICATIONS AND THE REACH TONNAGE BAND REGISTRATION

Substance	Abbreviation	CAS-no	Chemical structure	Harmonised Classification	Notified Classification	REACH registration (Tonnage band)
<b>2,4,6-Tribromophenol</b>	TBP (2,4,6-TBP)	118-79-6		No	Yes	1,000 -10,000 tpa
<b>Tri[3-bromo-2,2-bis(bromomethyl)propyl] phosphate</b>	TTBNPP	19186-97-1		No	No	0-10 tpa 1-10 tpa 100-1,000 tpa
<b>2-(2-Hydroxyethoxy)ethyl 2-hydroxypropyl 3,4,5,6-tetrabromophthalate</b>	HEEHP-TEBP	20566-35-2		No	Yes	10-100 tpa
<b>1,3,5-Triazine, 2,4,6-tris(2,4,6-tribromophenoxy)-</b>	TTBP-TAZ	25713-60-4		No	No	1,000-10,000 tpa

Substance	Abbreviation	CAS-no	Chemical structure	Harmonised Classification	Notified Classification	REACH registration (Tonnage band)
<b>Bis(2-ethylhexyl) tetra-bromophthalate</b>	BEH-TEBP (BEHTBP)	26040-51-7		No	Yes	100-1,000 tpa
<b>N,N'- ethylenebis(3,4,5,6-tetrabromophthalimide)</b>	EBTEBPI	32588-76-4		No	Yes	100-1,000 tpa
<b>2,2-bis(bromomethyl) propane-1,3-diol</b>	DBNPG	3296-90-0		No	Yes	100-1,000 tpa
<b>Tetrabromophthalic anhydride</b>	TEBP-Anh	632-79-1		No	Yes	10-100 tpa
<b>2-butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated</b>	-	68441-62-3		No	Yes	1,000-10,000 tpa

## 2. Results of registration data analysis

For each of the 9 BFRs, a data set with identification of the substance, important physical-chemical characteristics and the toxicological and ecotoxicological data is included in a data sheet for each of the 9 BFR substances (Annex 1). Data were extracted from the latest REACH disseminated registration dossiers on the ECHA homepage, which should be the latest and most updated data sets for these substances. Data were extracted from October to November 2014. For each endpoint, key studies, supplementary studies and weight of evidence studies from the registration are described.

Only studies with Klimisch scores of 1 and 2 have been included. The Klimisch score evaluates the inherent quality of a test report or publication in relation to standardised internationally recognised test guidelines and methodology. The following Klimisch scoring system is recognised:

1 = reliable without restrictions; 2 = reliable with restriction; 3 = not reliable and 4 = not assignable.

For each study, information on test method and guideline used, including information on test species, conditions, results, and references has been included in the evaluation. In the registration dossiers, some endpoints have been covered using read-across to similar substances. In these instances, this has been noted in the evaluation.

For the toxicological evaluation, the endpoints included in the evaluation are: Sensitisation, genotoxicity/mutagenicity, carcinogenicity, repeated dose toxicity (subchronic and chronic - NOAEL/LOAEL), reproductive/developmental (NOAEL/LOAEL), toxicokinetics, and data on possible endocrine disrupting effect (if available). For the endocrine endpoint, focus will be on data from studies investigating anogenital distance and nipple retention, i.e. an antiandrogen effect, results from the Uterotrophic assay indicative of an oestrogen activity and further hormonal data (TSH, T<sub>3</sub>, T<sub>4</sub>), gene expression analysis representing major pathways of male reproduction tract development, and data on the thyroid. Furthermore, the no effect levels (DNEL) derived by the registrant are also included.

For the ecotoxicological evaluation, focus has been on CLP, PBT assessment, environmental fate and pathways, and ecotoxicological information. The endpoints included in the evaluation are: stability, biodegradation, bioaccumulation (log K<sub>ow</sub>, BCF), adsorption/desorption, aquatic and terrestrial ecotoxicity (acute (EC/LC<sub>50</sub>) and chronic data (EC/LC<sub>10</sub> and NOEC)), and data on possible endocrine disrupting effect (if available). The derived predicted no effect concentration (PNEC) is also included if derived by registrant.

It has to be emphasised that all conclusions drawn in the registration dossiers are the responsibility of the registrants, and the results and conclusions drawn from these have therefore only been referenced in this evaluation. Thus, this evaluation should be seen as a pre-screening of the available data rather than an in-depth evaluation. The pre-screening has focused on data availability/data gaps and indications from the available data pointing towards a potential concern for CMR effects (including endocrine disruption) and PBT and vPvB effects

Based on the data sets in Annex 1, conclusions on the most important endpoints have been drawn and are summarised in Table 2 and Table 3 describing the key toxicological and ecotoxicological properties (the lowest NOAEL and critical effect is indicated). Also, an evaluation of the available data sets in terms of quality and completeness is included in Table 4.

**TABLE 2**

OVERVIEW OF MAIN TOXICOLOGICAL PROPERTIES FOR THE 9 BROMINATED FLAME RETARDANTS BASED ON DISSEMINATED REACH REGISTRATION DOSSIER DATA AVAILABLE ON THE ECHA HOMEPAGE. DATA WERE EXTRACTED FROM OCTOBER TO NOVEMBER 2014. THE INHERENT PROPERTIES OF THE 9 BROMINATED FLAME RETARDANTS ARE SUMMARISED FOR KEY PARAMETERS DESCRIBING THE LOWEST EFFECT CONCENTRATIONS: NOEL/NOEL FOR REPEATED DOSE TOXICITY, REPRODUCTIVE AND DEVELOPMENTAL TOXICITY AS WELL AS CARCINOGENICITY. DATA ON SKIN SENSITIZATION IS INCLUDED AS WELL AS DATA ON ENDOCRINE ENDPOINTS IF AVAILABLE. + = EFFECTS; - = NO EFFECT; LO = LOCAL EFFECTS; SY = SYSTEMIC TOXICITY; MA = MATERNAL TOXICITY; DE = DEVELOPMENTAL TOXICITY; ND = NO DATA

Substance	CAS	Sensitisation	Subchronic/ Chronic (mg/kg bw/day)  (mg/m <sup>3</sup> )	Carcinogenicity (mg/kg bw/day)	Mutagenicity / Genotoxicity	Reproductive toxicity (mg/kg bw/day)	Developmental toxicity (mg/kg bw/day)	Endocrine data
<b>TBP (2,4,6-TBP)</b>	118-79-6	Sens. (+)	NOAEL (28d) 50 (oral –LO) 150 (oral – SY)  NOEL (28d) 1000 (dermal)  NOEL (screening) 100 (GE)	ND	In vitro (-/+) In vivo (ND)	NOAEL (Fo) 1000	NOAEL (MA) 1000 NOAEL (DE) 300	No indication from OECD 422 screening study
<b>TTBNPP</b>	19186-97-1	Sens. (-)	NOAEL(90d) 1358-1658  NOAEL(28d) 1361-2081	ND	In vitro (-/+) In vivo (ND)	NOEC (FO) 1590/1775  NOEC (FI) 3040/3095	NOAEL (MA) 1000 NOAEL (DE) 300	No indication from OECD 421 screening study
<b>HEEHP-TEBP</b>	20566-35-2	ND	NOAEL(28d) 223 (oral) (RA)  NOEC (15d) 8 (inhalation) (RA)  NOAEL(20d) 500 (dermal) (RA)	NOAEL 50000 ppm (rat) (RA) 12500 ppm (mice) (RA)	In vitro (-) In vivo (ND)	ND	NOEL (MA) 3000 (RA)	No indication from OECD 407 (28d) – Negative for peroxisome proliferation
<b>TTBP-TAZ</b>	25713-60-4	Sens. (-)	NOEL(90d) 1000 (oral)  NOAEL(28d) 1000 (oral)	ND	In vitro (-) In vivo (ND)	ND (testing proposal)	NOAEL (MA) 1000 NOAEL (DE) 1000	No indication from OECD408 (90d) – No sperm count and mobility, oestrus cycle

1

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<b>BEH-TEBP (BEHTBP)</b>	26040-51-7	Sens. (-)	NOEL (28d) 223 (oral)	ND	In vitro (-/+) In vivo (-)	ND	ND (testing proposal)	No indication from OECD407 (28d) – reproductive organs, peroxisome proliferation
<b>EBTEBPI</b>	32588-76-4	ND	NOEL (28d) 1% /1000 (oral)	ND	In vitro (-) In vivo (ND)	ND	NOAEL (MA) 1000 NOAEL (DE) 1000 (rat/rabbit)	ND
<b>DBNPG</b>	3296-90-0	Sens. (-)	LOAEL (90d) 35-185 mg/kg bw/day	LOAEL 2500 ppm LOAEL 312 ppm	In vitro (+) In vivo (ND)	NOEL (Fo, F1, F2) 0.1%	ND	No indication from 2-gen. repro. study
<b>TEBP-Anh</b>	632-79-1	Sens. (+ in vitro ) Sens. (- /human)	NOAEL (90d) 1500 (oral) (RA)  NOAEC (15d) 2 (inhalation)  NOEL (screening) 500 (dermal)	ND	In vitro (+/-) In vivo (-)	ND	NOAEL (MA) 3000 NOAEL (DE) 3000  NOEL (MA) 1000 NOEL (DE) 1000 (RA)	No effects on sperm morphology and vaginal cytology evaluation
-	68441-62-3	Sens. (-)	LOAEL (14d) 417 (oral)  NOAEC (90d) 300 (inhalation)  NOEL (28/14d) 300 inhalation) 300 (inhalation)	ND	In vitro (+) In vivo (-)	ND	NOAEL (MA) 940 NOAEL (DE) 940	No effects on sperm counts; Effects on sperm morphology

**TABLE 3**

OVERVIEW OF THE MAIN PHYSICO-CHEMICAL AND ECOTOXICOLOGICAL PROPERTIES FOR THE 9 BROMINATED FLAME RETARDANTS BASED ON DISSEMINATED REACH REGISTRATION DOSSIER DATA AVAILABLE ON THE ECHA HOMEPAGE. DATA WERE EXTRACTED FROM OCTOBER TO NOVEMBER 2014. THE INHERENT PROPERTIES OF THE 9 BROMINATED FLAME RETARDANTS ARE SUMMARISED FOR KEY PARAMETERS DESCRIBING THE LOWEST EFFECT CONCENTRATIONS: LC50, LC10, EC50, NOEC FOR ALGAE, CRUSTACEANS AND FISH.

Substance	CAS	Biodegradability	Water solubility	log K <sub>ow</sub>	Bioaccumulation	Vapour pressure (Pa)	Lowest toxicity endpoint	Evaluation of PBT screening criteria <sup>3</sup>
TBP (2,4,6-TBP)	118-79-6	No information	50 mg/L (19 °C, pH: >6.9-<7)	3.7 (23.5 °C)	BAF = 20-140 Log BCF = 2.71	0.063 (25 °C)	EC50 ( <i>Daphnia magna</i> , 48 hours): 0.26 mg/L  NOEC ( <i>Daphnia magna</i> , 21d) = 150 µg/L (reproduction) ((NOEC (21d) = 25 µg/L (mortality))	P: No data B: Not fulfilled T: Not fulfilled (Corap: suspected PBT)
TTBNPP	19186-97-1	Not readily biodegradable (39 d, 37%)	0.0156 mg/L (20 °C, pH 6.7)	4.87 (25°C, pH >6-<7)	BCF <10 -200	3*10 <sup>-13</sup> (25 °C)	NOEC ( <i>Daphnia magna</i> , 16 days): = 3.200 µg/L (reproduction)	P: Fulfilled B: Not fulfilled T: Not fulfilled
HEEHP-TEBP	20566-35-2	Not readily biodegradable (QSAR)	0.05697 mg/L, (25°C)	>3.8	BCF = 390	0	LC50 (96 hours, <i>Lepomis macrochirus</i> ): 12 mg/L	P: Fulfilled B: Not fulfilled T: Not fulfilled (Only QSAR data for P)
TTBP-TAZ	25713-60-4	Not inherently biodegradable	< 0.001 mg/L (20°C)	8.63	-	1.52*10 <sup>-20</sup> (25°C)	>0.013 mg/L (E(L)C50: fish algae and crustacean) (above water solubility)	P: Fulfilled B: Fulfilled T: Not fulfilled (Only QSAR data for B)

<sup>3</sup> Evaluation of REACH registration data according to the screening criteria for PBT reported in the ECHA Guidance document R 11. (ECHA, 2014).

Substance	CAS	Biodegradability	Water solubility	log K <sub>ow</sub>	Bioaccumulation	Vapour pressure (Pa)	Lowest toxicity endpoint	Evaluation of PBT screening criteria <sup>3</sup>
BEH-TEBP (BEHTBP)	26040-51-7	Not inherently biodegradable (7%, 28d)	Insoluble (< 0.1 mg/L)	10.2 (25 °C, pH 6.1)	BMF: 0.014-0.0012.	3.56*10 <sup>-7</sup> (25 °C)	EC50 ( <i>Daphnia magna</i> , 48 hours): >10 mg/L NOEC ( <i>Daphnia magna</i> , 21 days): >= 1 mg/L EC10 ( <i>Desmodesmus subspicatus</i> , 72 hours): >100 mg/L	P: Fulfilled B: Not fulfilled T: Not fulfilled
EBTEBPI	32588-76-4	Not readily biodegradable (0%, 14d)	< 1 mg/L, ambient air temperature	-	BCF =0.3-3.3	2.27*10 <sup>-4</sup>	LC50 ( <i>Oryzias latipes</i> , 48 hours): >500 mg/L	P: Fulfilled B: Not fulfilled T: Not fulfilled
DBNPG	3296-90-0	Not readily biodegradable (25%, 28d) Inherently biodegradable (44%, 33d)	19.4 g/L (20±0.5°C)	1.08	1.1-<4.8	2*10 <sup>-3</sup>	EC50 ( <i>Desmodesmus subspicatus</i> , 72 hours): 37 mg/L NOEC ( <i>Desmodesmus subspicatus</i> , 72 hours): 12.5 mg/L	P: Fulfilled B: Not fulfilled T: Maybe fulfilled if classified as Carc. 1b. )
TEBP-Anh	632-79-1	Not readily biodegradable	241 mg/L (25 °C)	1.98	0	2.73*10 <sup>-6</sup>	EC50 ( <i>Daphnia magna</i> , 48 hours): > 5.6 mg/L LC50 ( <i>Oncorhynchus mykiss</i> , 96 hours): > 10 mg/L	P: Fulfilled B: Not fulfilled T: Not fulfilled. (Only QSAR data for P)
-	68441-62-3	Not readily biodegradable (16%, 28d)	4.4 g/L (20°C, pH 3.6)	-0.03-3.3 (25°C, pH7)	-	0.0655 (20°C)	NOEC ( <i>Pseudokirchnerella subcapitata</i> , 96 hours): 250 mg/L (growth rate)	P: Fulfilled B: Not fulfilled T: Not fulfilled.



# 3. Analysis of data in the registration dossiers

Publicly available data on the toxicity and ecotoxicity of 9 BFRs were extracted/compiled from the latest REACH registration dossiers on the ECHA homepage. Data were extracted from October to November 2014. For each of the (eco) toxicity endpoints, only the studies identified by the registrant as key studies, supplementary studies and weight of evidence studies (if evaluated to be needed in the overall conclusion when data not sufficient from key studies) from the registration are described. Studies specifically addressing combinatory effects were not available. Only studies with Klimisch scores of 1 and 2 are included. The Klimisch scores of 1 and 2 indicate that the data were of good quality, usually test data from studies performed in accordance with internationally recognised test guidelines (or similar to) and GLP regulations.

It should be noted that read-across (RA) approaches were used in the registration dossier for a few of the BFRs and for others, further proposals for testing were included by the registrant.

It should be noted that for none of the substances there were data or discussion of possible endocrine disrupting properties or on combination effects with similar substances. Further, no testing proposals were made specifically addressing endocrine disrupting effects.

The DNEL-values derived by the registrants are referred both in the separate datasheets (Annex 1) and in the summary table below (Table 4). In this table, key toxicological endpoints are summarised and data gaps identified in relation to the data requirements for a full REACH registration, i.e. the best obtainable database for a complete hazard characterisation of all end-points (> 1000 tpa, Annex X). Further, the lowest N(L)OAL -values for critical endpoints are included as well as the derived oral DNELs for general population.

## 3.1 Toxicological properties of the 9 BFRs

Toxicological profiles for the 9 BFRs have been established. These are reported in separate datasheets (Annex 1) and summary Tables 2 and 4. Based on this the hazard profiles can be shortly described for each h of the substances:

For **TBP (2,4,6-TBP) (CAS: 118-79-6)**, the REACH registration dossier (tonnage band 1000-10 000 tonnes) indicated a positive response to skin sensitisation (The registrant has classified as Skin Sens. 1 (H317) based on positive test data), a NOAEL of 50 mg/kg bw/day (28-day) based on local toxicity (gastric) and a NOEL of 100 mg/kg bw/day for repeated dose toxicity (liver/kidney toxicity) and NOAEL of 1000 mg/kg bw/day for reproductive toxicity and 300 mg/kg bw/day (growth/number of live pups) from a screening study (combined repeated dose/reproduction toxicity study).

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study, prenatal studies or carcinogenicity study were available. Data for *in vitro* and *in vivo* genotoxicity available showing clastogenic effects *in vitro* but no effects *in vivo* (chromosome aberration). In terms of a possible endocrine activity, no data were available in the registration dossier. Thus, important data are needed in terms of reproductive toxicity (multi-generation study) and prenatal toxicity studies to further evaluate fertility and developmental effects and endocrine activity. Further, no carcinogenicity data are available from the registration dossier.

Overall, limited data are available in terms of CMR properties and repeated dose toxicity; however no serious alert from existing data. *Nevertheless, it should be noted that TBP (2,4,6-TBP) is on the CoRap-list for further evaluation (status is ongoing) due to suspected CMR properties.*

For **TTBNPP (CAS: 19186-97-1)** the REACH registration dossier (tonnage band 100-1000 tonnes) indicated a negative response to skin sensitisation. A NOAEL of 1361-2081 mg/kg bw/day (28-day) and a NOAEL of 1361-1658 mg/kg bw/day (90-day) for repeated dose toxicity was indicated. Further, no effects in a reproduction/developmental screening study (NOEC of 1590-4110 mg/kg bw/day –Fo/F1). A NOAEL of 300 mg/kg bw/day (foetal weight) was identified in a developmental toxicity study.

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study, prenatal studies or carcinogenicity study were available. No genotoxicity observed *in vitro*, however, data on *in vivo* genotoxicity lacking. In terms of a possible endocrine activity, no data were available in the registration dossier. Thus, important data are needed in terms of reproductive toxicity (multi-generation study) and prenatal toxicity studies (rabbit) to further evaluate fertility and developmental effects and endocrine activity. Further, no carcinogenicity data are available from the registration dossier.

Overall, limited data are available in terms of CMR properties and repeated dose toxicity, however, no specific alert from existing data. The registrant has not classified the substance.

For **HEEHP-TEBP (CAS: 20566-35-2)**, the REACH registration dossier (tonnage band 10-100 tonnes) indicated no data on skin sensitisation. Using read-across to the structural analogue Tetrabromophthalic anhydride (CAS 632-79-1) the registrant included the following data: a NOEC of 8 mg/m<sup>3</sup> (15d, inhalation) and a NOAEL of 500 mg/kg bw/day (20d, dermal) for repeated dose toxicity. Using read-across to the structural analogue BEH-TEBP (BEHTBP) (CAS 26040-51-7), the registrant included the following data: A NOAEL of 2000 ppm (Approx. 223 mg/kg bw/day) (28-day, oral, OECD 407). In the oral 28-day study, a positive control group (DEHP – 15000 ppm) was included. The positive control group produced marked signs of toxicity. No data on reproductive toxicity but a NOEL of 3000 mg/kg bw/day was identified from a developmental toxicity study using read-across to Tetrabromophthalic anhydride (CAS 632-79-1).

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study and prenatal study (rat) available. In terms of carcinogenicity, a NOAEL of 12500-50000 ppm was identified using read-across to phthalic anhydride (CAS 85-44-9). Limited *in vitro* data available, showing no genotoxicity. No *in vivo* genotoxicity data. In terms of a possible endocrine activity, no data were available in the registration dossier. Thus, important data are needed in terms of reproductive toxicity (multi-generation study) and prenatal toxicity study (rat) to further evaluate fertility and developmental effects and endocrine activity.

Overall, very limited specific data on the substance and the data (in terms of CMR properties and repeated dose toxicity) is primary based on read-across to structural analogues (tetrabromophthalic anhydride CAS 632-79-1 ; bis(2-ethylhexyl) tetrabromophthalate CAS 26040-51-7; BEH-TEBP (BEHTBP) (CAS: 26040-51-7) and phthalic anhydride (CAS 85-44-9)) are available, however no serious alert from these data. The registrant has not classified the substance.

For **TTBP-TAZ (CAS: 25713-60-4)**, the REACH registration dossier (tonnage band 1000-10 000 tonnes) indicated no skin sensitisation. A NOEL of 1000 mg/kg bw/day (28d) and a NOAEL of 1000 mg/kg bw/day (90d) was identified from repeated dose toxicity. Further, a NOAEL of 1000 mg/kg bw/day for developmental toxicity was identified. No data on reproductive toxicity, the registrant has proposed a two-generation reproduction study to ECHA.

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study, prenatal study (rabbit) or carcinogenicity study were available. Data for *in vitro* showed no genotoxicity. No data for *in vivo* genotoxicity available. In terms of a possible endocrine activity, no data were available in the registration dossier. Thus, important data are needed in terms of reproductive toxicity (multi-

generation study) and prenatal toxicity studies to further evaluate fertility and developmental effects and endocrine activity. Further no carcinogenicity data available from the registration dossier.

Overall, limited data are available in terms of CMR properties and repeated dose toxicity, however, no specific alert from existing data. The registrant has proposed a two-generation reproduction study. The registrant has not classified the substance.

For **BEH-TEBP (BEHTBP) (CAS: 26040-51-7)**, the REACH registration dossier (tonnage band 100-1000 tonnes) indicated no skin sensitisation. A NOAEL of 223 mg/kg bw/day (28-day) was identified for repeated dose toxicity (body weight gain). There is no specific fertility study with BEHTBP available. In the 28-day study, no effects on reproductive organs were observed. The pathological evaluation covered organ weight, gross and microscopic examination of reproductive organs, incl. epididymides, mammary glands - caudal, ovaries, prostate, testes, and uterus (with cervix). No treatment-related changes were observed for any reproductive organ investigated during macroscopic and microscopic examination. A positive control group (DEHP - ca. 1507 mg/kg bw) was included in the 28-day study. Organ weight analysis for the DEHP group indicated low testes weights with small, flaccid testes and histopathological a lack of germinal epithelium in the testes. No data on developmental toxicity, the registrant has proposed a developmental toxicity to ECHA.

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study, prenatal studies or carcinogenicity study were available. Data for *in vitro* genotoxicity showed effect on chromosome aberration (clastogenic activity) but no effects in gene mutation assays (Ames tests). No genotoxicity *in vivo* (Micronucleus Assay). In terms of a possible endocrine activity, no data were available in the registration dossier. *In vitro* data on concentration-dependent effects on overt toxicity and hepatic messenger RNA (mRNA) expression levels of 11 transcripts in primary cultures of chicken embryonic hepatocytes (CEH) was negative. Thus, important data are needed in terms of reproductive toxicity (multi-generation study) and prenatal toxicity studies to further evaluate fertility and developmental effects and endocrine activity. Further no carcinogenicity data available from the registration dossier.

Overall, very sparse data are available from the REACH registration dossier on BEHTBP in terms of repeated dose toxicity, reproductive toxicity and endocrine activity (CMR properties), however, no serious alert from existing data. The registrant has proposed a developmental toxicity. The registrant has not classified the substance.

For **EBTEBPI (CAS: 32588-76-4)**, the REACH registration dossier (tonnage band 100-1000 tonnes) indicated no data for skin sensitisation. A NOAEL of 1% in diet (approx. 1000 mg/kg bw/day) was identified for 28d and 90d repeated dose studies. No data for reproductive toxicity. A NOEL of 1000 mg/kg bw/day was identified for developmental toxicity in rats and rabbits.

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study or carcinogenicity study were available. Data for *in vitro* genotoxicity showed no mutagenic effects (Ames test) and no clastogenic activity (chromosome aberration). No data on *in vivo* genotoxicity. In terms of a possible endocrine activity, no data were available in the registration dossier. Thus, important data are needed in terms of reproductive toxicity (multi-generation study) to evaluate fertility and endocrine activity. Further no carcinogenicity data available from the registration dossier.

Overall, limited data are available in terms of CMR properties and repeated dose toxicity, however, no serious alert from existing data. The registrant has not classified the substance.

For **DBNPG (CAS: 3296-90-0)**, the REACH registration dossier (tonnage band 100-1000 tonnes) indicated no to skin sensitisation. A LOAEL of 312-2500 ppm corresponding to 35-185 mg/kg bw/day using mice/rats (90d in a combined chronic toxicity/carcinogenicity study) was identified for repeated dose toxicity (systemic effects). A NOEL of 0.1% for

reproductive toxicity (P. F1, F2) was identified from a two-generation reproduction toxicity study in mice (at the 0.4% dose level, reproduction was adversely affected). No data on developmental toxicity.

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no prenatal studies were available. Data for *in vitro* genotoxicity showed mutagenic effects (Ames test), clastogenic effects (chromosome aberration) and possible gene mutations (sister chromatid exchanges). No data on *in vivo* genotoxicity. *Clear carcinogenic effects* were seen in a combined chronic toxicity/carcinogenicity study. A LOAEL of 312-2500 ppm corresponding to 35-185 mg/kg bw/day using mice/rats for carcinogenic effects in mice and rats was identified. In terms of a possible endocrine activity, no data were available in the registration dossier. Thus, important data are needed in terms of prenatal toxicity studies to evaluate developmental effects and studies investigating endocrine activity.

Overall, data are available in terms of CMR properties, repeated dose toxicity but not for developmental toxicity. Clear carcinogenic and reproductive effects were seen. The registrant has classified as Carc. 2 (H351).

For **TEBP-Anh (CAS: 632-79-1)**, the REACH registration dossier (tonnage band 1-10 tonnes) indicated a positive response to skin sensitisation based on animal data (Klimisch score 1) and negative in human patch test (Klimisch score 2), hence an overall positive response to skin sensitization as indicated by registrant (Skin Sens. 1). In repeated dose toxicity studies using read-across to tetrachlorophthalic anhydride [117-08-8], a NOAEL of 1500 mg/kg bw/day (90d) was observed in mice but a LOAEL of 94 mg/kg bw/day (90d - oral) was observed in rats in same type of study with same dosing regimen based on renal toxicity. Further, a NOAEC of 2 mg/m<sup>3</sup> (15d - inhalation) and a NOAEL of 500 mg/kg bw/day (20d) was identified. No data on reproductive toxicity. A NOEL of 1000 mg/kg bw/day was identified for developmental toxicity using rats; the same result obtained using read-across to tetrachlorophthalic anhydride [117-08-8].

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study, prenatal study (rabbit) or carcinogenicity study were available. No *in vitro* genotoxicity identified from mutation (Ames test) and clastogenic activity (chromosome aberration) assays. No *in vivo* genotoxicity identified from chromosome aberration and gene mutation assays (micronucleus and sex-linked lethal mutation) but ambiguous in another chromosome aberration assay. Overall, important data are needed in terms of reproductive toxicity (multi-generation study) to further evaluate fertility and endocrine activity. Further no carcinogenicity data available from the registration dossier.

Overall, limited data are available in terms of CMR properties and repeated dose toxicity, however no serious alert from existing data. The registrant has classified as Skin Sens. 1 (H317) based on positive test data.

For **CAS No 68441-62-3**, the REACH registration dossier (tonnage band 1000-10 000 tonnes) indicated a negative response to skin sensitisation. In terms of repeated dose toxicity, A LOAEL of 417 mg/kg bw/day (14d-oral) was identified based on liver and thyroid weight changes, a NOAEC of 300 mg/m<sup>3</sup> (90d and 28d–inhalation, systemic effects) and a LOAEC of 300 mg/m<sup>3</sup> (28d–inhalation, local effects). No data on reproductive toxicity, the registrant has proposed a two-generation reproduction toxicity study to ECHA. A NOEL of 940 mg/kg bw/day was identified for developmental toxicity. A second developmental toxicity study in rabbits has been proposed to ECHA by the registrant. The substance was positive for genotoxicity *in vitro* in the Ames test and the cell gene mutation assay but negative *in vivo* (UDS test and micronucleus assay). No data on carcinogenicity.

The data set from the registration dossier was not adequate for a high tonnage registration (Annex X: > 1000 tpa.), i.e. no two-generation reproduction toxicity study, no rabbit prenatal study or carcinogenicity study were available. Thus, important data are needed in terms of reproductive toxicity (multi-generation study) and prenatal toxicity studies to further evaluate fertility and developmental effects and endocrine activity.

Overall, limited data are available in terms of CMR properties and repeated dose toxicity, however no serious alert from existing data. A two-generation study and a developmental toxicity study has been proposed by the registrant.

### 3.2 Ecotoxicological properties of the 9 BFRs

Environmental profiles for the 9 BFRs have been established. These are reported in separate datasheets (Annex 1) and summary Tables 3 and 4. The environmental profiles can be divided into environmental fate properties and hazard profile properties:

For **TBP (2,4,6-TBP) (CAS: 118-79-6)** there is no information on biodegradability. TBP is water soluble (50 mg/L at 19°C) and has a Log Kow of 3.7 at 23.5 °C. Furthermore, a BAF (3 days) of 20-140 is reported based on a key-study with fish. The vapour pressure is reported as 0.063 Pa at 25 °C. A Henry law constant (H) describing the volatility in water, was not reported. The highest acute toxicity is observed for *Daphnia magna* where an EC<sub>50</sub> (48h) of 0.26 mg/L is available. Furthermore, a chronic NOEC (*Daphnia magna*, 21d) of 150 µg/L and 25 µg/L is reported based on the endpoint reproduction and mortality respectively. No long term study is available for fish. The PNEC for freshwater and marine water are reported as 0.5 µg/L and 0.05 µg/L, respectively. Data on the terrestrial toxicity are available for soil macroorganisms only. A NOEC (Earthworm, 14d) = 100 mg/kg soil dw is reported and a PNEC<sub>soil</sub> of 201 µg/kg soil dw. According to the registrant TBP is not a PBT substance, however, a CORAP is available where TBP is reported as a *suspected* PBT substance.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline<sup>4</sup>, TBP does not fulfil the screening criteria for B and T. Criteria for P cannot be assessed due to the lack of data.

For **TTBNPP (19186-97-1)** 37% degradation was obtained after 39 days. Therefore TTBNPP cannot be considered as readily biodegradable. The water solubility at 20 °C was reported as 0.0156 mg/L and a Log Kow of 4.87 (25 °C) and a BCF of <10-200 was reported. The vapour pressure is reported to be 3\*10<sup>-13</sup> Pa at 25 °C. A Henry law constant (H) describing the volatility in water, was not reported. Acute toxicity for all trophic levels (algae, crustacean and fish) is reported as EC<sub>50</sub> > 100 mg/L. The highest toxicity is observed for *Daphnia magna* where a NOEC (16d) of 3.200 µg/L is reported based on the endpoint reproduction. The endpoint study was conducted according to the OECD Guideline no 202, which is the guideline for acute toxicity. However, the endpoint “reproduction” and the duration of 16 days (normally 21 days is applied in the OECD guideline no. 211) are approximately in accordance with a chronic toxicity study. No long term study is available for fish. The PNEC for freshwater and marine water are reported as 0.000312 mg/L and 0.0000312 mg/L respectively. Data on the terrestrial toxicity are reported for plants and soil macroorganisms. The highest toxicity is reported for plants where a NOEC (21d, *Allium cepa*) < 0.1 mg/L is reported. The PNEC<sub>soil</sub> is reported as 1 µg/kg soil dw. According to the registrant, TTBNPP is not a PBT substance.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline R.11 ((ECHA, 2012), TTBNPP does fulfil the screening criteria for P (not readily biodegradable) but not the criteria for B and T.

**HEEHP-TEBP (CAS: 20566-35-2)** is not expected to be readily biodegradable based on QSAR (BIOWIN) calculations. Based on QSAR calculations the estimated water solubility is reported as 0.05697 mg/L (25°C). A Log Kow of > 3.8 and a BCF of 390 were estimated for HEEHP-TEBP. Furthermore, a vapour pressure of 0 Pa has been calculated. A Henry law constant (H) describing the volatility in water, was not reported. Only QSAR calculations are available for algae and crustaceans. The LC<sub>50</sub> of 12 mg/L for fish was however based on an experimental study (96 hours, *Lepomis macrochirus*). No long term studies are available. A QSAR calculation reports a chronic value (Chv) for fish of 0.0447 mg/L. The PNEC for freshwater, is reported as 0.011 mg/L. No PNEC is reported for marine water. No data on the terrestrial toxicity have been reported.

According to the registrant HEEHP-TEBP is not a PBT substance. They conclude that the substance does display properties that indicate persistency within the environment, based on the EPIWIN BIOWIN. A calculated assessment of bioaccumulation produced a BCF value of 390 indicating that the substance does not fulfil the screening criteria for

<sup>4</sup> Guidance on Information Requirements and Chemical Safety Assessment. Chapter R.11 : PBT/vPvB Assessment. European Chemicals Agency, 2014

bioaccumulation. The substance did not cause any hazardous effects to any of the trophic levels in the aquatic organisms at the limit of solubility in water and in any of the mammalian studies conducted on the substance.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT, HEEHP-TEBP does not fulfil the screening criteria for P (however only QSAR), B (only calculated value) and T.

**TTBP-TAZ (CAS: 25713-60-4)** is not inherently biodegradable (39d, 4%). The water solubility was reported as < 0.001 mg/L (20°C) and a Log Kow of 8.63 was calculated applying QSAR calculations. No BCF value is reported (test inconclusive). The vapour pressure of TTBP-TAZ is  $1.52 \times 10^{-20}$  Pa (25°C). A Henry law constant (H) describing the volatility in water, was not reported. Acute toxicity data for all three trophic levels (algae, crustacean and fish) are reported as > 0.013 mg/L. No data on chronic toxicity is reported for TTBP-TAZ. The PNEC for freshwater and marine water are reported as 0.00001 mg/L and 0.000001 mg/L respectively. Data on the terrestrial toxicity are reported for plants and soil macroorganisms. The highest toxicity was obtained for plants where a NOEC (*Lycopersicon esculentum*, 21 days) > 2.3 mg/kg soil dw. is reported. The PNECsoil is reported as 0.246 mg/kg soil dw.

According to the registrant TTBP-TAZ is not a PBT substance. They conclude that the DT50 calculated from the simulation studies exceeded 180 day and therefore the test substance could be considered as very persistent (vP). During the bioconcentration test with fish, exposed to 0.5 mg/L which was above the maximum level of water solubility of the substance no conclusive results could be obtained. However, studies with rat indicated negligible uptake of the substance and therefore the substance was concluded to be not bioaccumulative. No toxicity was observed (tests were conducted at a concentration corresponding to the water solubility) and the substance is not a CMR substance; therefore it was not considered a T substance.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT assessment, TTBP-TAZ does fulfil the screening criteria for P, vP and B(vB) (Log Kow based on QSAR) but not T... For TTBP-TAZ, an RMOA is being performed at the moment based on *suspected* PBT properties.

**BEH-TEBP (BEHTBP) (CAS: 26040-51-7)** is not inherently biodegradable (7%, 28d). The water solubility of the substance could not be detected without solubilizer and is reported to be low (< 0.05 µg/L). The Log Kow is reported as 10.2 and a BMF of 0.0012-0.014 is reported based on a study with fish. The vapour pressure was estimated applying QSAR calculations and is reported as 0.00000356 Pa (25 °C). A Henry law constant (H) describing the volatility in water, was not reported. The acute toxicity to algae, crustacean and fish is reported together with chronic toxicity studies for crustacean and algae. The highest toxicity was reported for the crustacean where NOEC (21d, *Daphnia magna*) of ≥ 1 mg/L is available. No chronic data are available for fish and no data on the terrestrial toxicity are reported. No PNEC values have been calculated for BEH-TEBP.

According to the registrant BEH-TEBP is not a PBT substance. They conclude that the substance is not considered persistent based on rapid hydrolysis. It should be noted, however, that the substance is not inherently biodegradable (only 7% biodegradation after 28 days) and the rapid hydrolysis might reflect an initial transformation into non-degradable substances. Thus the hydrolysis does not reflect a complete degradation of BEH-TEBP and cannot be used as parameter for assessing PBT properties. The substance is further not bioaccumulative based on the BMF of 0.0012-0.0014 obtained in the study with fish, and not toxic since no toxic effects were obtained against daphnia and algae during the limit tests concentration which reflects the maximum water solubility under exposure conditions in both studies.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT assessment, BEH-TEBP does fulfil the screening criteria for P but not B and T. However, recent data indicate that BEH-TEBP can be

detected in air and biota<sup>5</sup>, indicating a bioaccumulation potential. Overall, further studies confirming bioaccumulation in aquatic species should be considered, alternatively further environmental monitoring.

**EBTEBPI (CAS: 32588-76-4)** is not readily biodegradable (0%, 14d). The water solubility is reported as < 1 mg/L at ambient air temperature and a vapour pressure of 0.000227 Pa at 20 °C. A Henry law constant (H) describing the volatility in water, was not reported. A Log Kow value was not reported for EBTEBPI however a BCF of 0.3-3.3 was reported for fish. No studies are available describing the toxicity towards algae and crustaceans. For fish only an acute toxicity study is available where the LC<sub>50</sub> (*Oryzias latipes*, 48 hours) is reported as >500 mg/L. No data on the terrestrial toxicity are reported. No PNEC values have been calculated for EBTEBPI. According to the registrant EBTEBPI is not a PBT substance.

The registrant conclude: A Level III Fugacity Model, based on chemical structure alone, estimates half-lives of 6.5 hr (air), 4320 hr (water), 8640 hr (soil) and 38900 hr (sediment) following emissions of 1000 kg/hr to each of air, water and soil. Overall persistence time is estimated at 5510 hrs or 7.6 months. That is, reaction with hydroxyl radicals in air is expected, and hydrolysis in water or biodegradation in soil and sediment is not expected. The substance is expected to partition predominantly to soil, where it is expected to be very persistent (vP). As the substance is insoluble, has a large molecular size and high molecular weight, and because its folded confirmation adversely affect its bioavailability it is not considered bioaccumulative. Furthermore, it did not bioconcentrate in fish when exposed via water which also indicates that the substance is not bioaccumulative. Furthermore, the substance was not acutely toxic to fish and it does not classify as CMR therefore it is not a T substance.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT assessment, EBTEBPI does fulfil the screening criteria for P (not ready biodegradable) but not B and T.

**DBNPG (CAS: 3296-90-0)** is not readily biodegradable (25%, 28d) but can be considered as inherently biodegradable (44%, 33d). DBNPG is water soluble (19.4 g/L (20±0.5°C)) and has a reported Log Kow of 1.08 and a BCF of 1.1-<4.8 (MITI). The vapour pressure is reported as 2\*10<sup>-3</sup> Pa (25 °C). A Henry law constant (H) describing the volatility in water, was not reported. The highest toxicity is reported for algae where an EC<sub>50</sub> = 37 mg/L and a NOEC of 12.5 mg/L is reported. Only acute toxicity data are available for crustaceans and fish. The PNEC for freshwater and marine water are reported as 0.037 mg/L and 0.0037 mg/L respectively. No data on the terrestrial toxicity are reported.

In the registration dossier a PBT (vPvB) assessment has not been included.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT assessment, DBNPG does fulfil the screening criteria for P (not ready biodegradable and inherently biodegradability is < 70%) and T (if classified as Carc. 1b.) but not B.

**TEBP-Anh (CAS: 632-79-1)** is not expected to be biodegradable based on QSAR calculations. TEBP-Anh is water soluble 241 mg/L (25 °C) and has a Log Kow of 1.98 and a BCF of 0 was derived using a flow through study with fish. The vapour pressure was estimated to be ca. 0.0000273 Pa and the Henry law constant was estimated to be 0.016Pa m<sup>3</sup>/mol using QSAR calculations. Experimental data on the acute toxicity are available for fish and crustacean. Data for algae and chronic data for crustaceans and fish have been estimated applying QSAR calculations. The EC<sub>50</sub> (*Daphnia magna*, 48 hours) was reported as > 5.6 mg/L and the corresponding PNEC for freshwater and marine water are reported as 0.0056 mg/L and 0.00056 mg/L respectively. No data on the terrestrial toxicity are reported.

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<sup>5</sup> Vorkamp *et al.*, (2015). Novel brominated flame retardants and dechlorane plus in Greenland air and biota. Environmental Pollution 196 (2015) 284e291

According to the registrant TEBP-Anh is not a PBT substance. They conclude that the primary route of environmental degradation is rapid hydrolysis to tetrabromophthalic acid therefore the substance is not considered to be persistent. The substance did not bioconcentrate in fish, and hydrolysis in water to the acid is expected. No toxicity was observed and substance is not classified as CMR.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT assessment, TEBP-Anh does fulfil the screening criteria for P (not ready biodegradable) but not B and T.

**2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS: 68441-62-3)** is not readily biodegradable (16%, 28d). The substance is water soluble 4.4 g/L (20°C, pH 3.6) and has a Log Kow of -0.03-3.3 (25°C, pH7); no BCF is available. The vapour pressure is 0.0655 Pa at (20°C). A Henry law constant (H) describing the volatility in water, was not reported. Acute toxicity studies are available for algae, crustacean and fish. No chronic studies (except algae) are available. The highest toxicity reported is for algae where a NOEC = 250 mg/L (*Pseudokirchnerella subcapitata*, 96 hours), is reported based on growth rate. The PNEC for freshwater and marine water are reported as 0.52 mg/L and 0.052 mg/L and are based on the reported endpoint for crustaceans; EC50 (*Daphnia magna* 48 hours) = 520 mg/L. No data on the terrestrial toxicity are reported.

According to the registrant (CAS: 68441-62-3) is not a PBT substance. They conclude that the substance is considered as hydrolytically stable and is not ready biodegradable and as potentially persistent in the environment as a worst-case assessment. The Log Kow was below 4.5 and therefore the substance is not a suspected B substance. The NOEC obtained in the study with algae is much higher than the screening criterion of 0.01 mg/l and the substance is not classified as being CMR. It is therefore not considered as a suspected T substance.

According to the data reported above and the PBT screening criteria reported in ECHA Guideline on PBT assessment, 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated does fulfil the screening criteria for P (not ready biodegradable) but not B and T.



**TABLE 4**  
 OVERVIEW OF MAIN TOXICOLOGICAL AND ECOTOXICOLOGICAL PROPERTIES FOR THE 9 BROMINATED FLAME RETARDANTS INCLUDING DERIVED LOWEST NOEL/NOEL VALUE FOR CRITICAL ENDPOINT. THE DNEL VALUES FOR THE GENERAL POPULATION AND THE PBT/vPvB ASSESSMENT IS INDICATED AS CONCLUDED BY THE REGISTRANT

Substance	CAS No	Sensitisation (S)	Carcinogenicity (C) Mutagenicity (M)	Repro toxicity (R) Dev toxicity (D)	Sub-/chronic toxicity	Endocrine activity	Lowest NOAEL (critical endpoint)	DNELs (general population)	PBT/vPvB assessment
TBP (2,4,6-TBP)	118-79-6	+++ /+++	o/o (C) ++ /++ (M)	+ /o (R) + /++ (D)	+ /++	o /o	NOAEL 50 mg/kg bw/day (Local-gastric)	0.25 mg/kg bw/day	No (On CoRap list)
(Skin. Sens. 1)									
TTBNPP	19186-97-1	+++ /o	o/o (C) + /o (M)	++ /o (R) ++ /+ (D)	+ /o	o /o	NOAEL 300 mg/kg bw/day (development)	7 mg/kg bw/day	No
HEEHP-TEBP	20566-35-2	o /o	(++) /o (C) (RA) + /o (M)	o /o (R) (+) /o (D) (RA)	(+) /++ (RA)	o /o	NOAEL 2000 ppm (diet) (systemic) (RA)	ND	No
TTBP-TAZ	25713-60-4	+++ /o	o/o (C) + /o (M)	o /o (R)* ++ /o (D)*	++ /o	o /o	NOAEL 1000 mg/kg bw/day	1.7 mg/kg bw/day	No (however vP, (P) and B substance) (RMOA evaluation)
BEH-TEBP (BEHTBP)	26040-51-7	+++ /o	o/o (C) ++ /+ (M)	o /o (R) o /o (D)**	+ /+	o /o	NOAEL 223 mg/kg bw/day (systemic)	0.37 mg/kg bw/day	No
EBTEBPI	32588-76-4	o /o	o/o (C) + /o (M)	o /o (R) ++ /o (D)	++ /+	o /o	NOAEL 1000 mg/kg bw/day	ND	No
DBNPG	3296-90-0	+++ /o	+++ /+++ (C) + /++ (M)	+++ /++ (R) + /++ (D)	+++ /+++	o /o	LOAEL 35 mg/kg bw/day (carc.)	ND	No
(Carc. 2)									
ε									
ε									

Substance	CAS No	Sensitisation (S)	Carcinogenicity (C) Mutagenicity (M)	Repro toxicity (R) Dev toxicity (D)	Sub-/chronic toxicity	Endocrine activity	Lowest NOAEL ( critical endpoint)	DNELs (general population)	PBT/vPvB assessment
TEBP-Anh	632-79-1	+++ /+++  (Skin. Sens. 1)	o/o (C)  ++/+ (M) (RA)	o/o (R)  + /+++ (D)	(++) / (+++) (RA)	o/o	LOAEL 94 mg/kg bw/day (Kidney) (RA)	ND	No
	68441-62-3	+++ /o	o/o (C)  ++ /++ (M)	o/o (R)***  ++ /o (D)***	++ /++	+ /+	NOAEC 300 mg/m <sup>3</sup> (Kidney)	0.4 mg/kg bw/day	No

**NOTES TO TABLE:** THE INHERENT PROPERTIES FOR THE INVESTIGATED SUBSTANCES ARE SUMMARISED USING KEY PARAMETERS: ACUTE AND LOCAL EFFECTS, SENSITISATION, CARCINOGENICITY(C), MUTAGENIC TOXICITY (M), REPRODUCTIVE TOXICITY (R), ENDOCRINE ACTIVITY, PBT/VPBT ASSESSMENT. THE FOLLOWING SYMBOLS ARE USED:

/ = DATA AVAILABILITY/EFFECT WITH THE FOLLOWING SCORE SYSTEM:

o = NO DATA/NO EFFECT

+ = ONLY IN VITRO STUDIES (MUT) OR FEW IN VIVO DATA (REPRODUCTION AND REPEATED DOSE)/SLIGHT EFFECT

++ = IN VITRO AND-OR SOME IN VIVO STUDIES/MODERAT EFFECT (NO CLASSIFICATION)

+++ = SUFFICIENT DATA SET/CLEAR EFFECT (CLASSIFICATION)

NC = NO CLASSIFICATION

WE = WEIGHT OF EVIDENCE

RA = READ-ACROSS

( ) = INDICATES THAT THE VALIDITY OF READ-ACROSS APPROACH HAS NOT BEEN EVALUATED

\* TWO-GENERATION REPRODUCTION STUDY AND A DEVELOPMENTAL TOXICITY STUDY PLANNED

\*\* A DEVELOPMENTAL TOXICITY STUDY PLANNED

\*\*\* TWO-GENERATION REPRODUCTION STUDY AND A DEVELOPMENTAL TOXICITY STUDY PLANNED

# 4. Discussion and conclusion

Below in section 4.1 is an evaluation and identification of data gaps in relation to critical endpoints given. Based on this and the information given in summary Tables 2, 3 and 4, overall conclusions are given for each of the BFR concerning the need for further substance evaluation

## 4.1 Critical effects of the 9 BFRs

Evaluations of the 9 BFRs have been based on the study summaries and conclusions drawn in the disseminated registration dossiers on the ECHA homepage. For each endpoint, key studies, supplementary studies and weight of evidence studies from the registration are described. Studies with Klimisch scores of 1 and 2 were preferred in the analysis. The disseminated registration dossiers on the ECHA homepage contain the most recent data set of the 9 BFRs in terms of toxicological and ecotoxicological properties submitted by the registrant. It must be emphasised that all conclusions drawn in the registration dossiers are the responsibility of the registrants, and the results and conclusions drawn from these in terms of no-effect level setting, DNELs/PNECs and the use of read-across have been used in this report with reference to the registration dossier. This pre-screening has focused on data availability/data gaps and indications from the available data pointing towards a potential concern for CMR effects (including endocrine disruption) and PBT and vPvB effects according to ECHA's Guidance Document R 11 (2014). Specifically, read-across approaches used by the registrant were pre-evaluated.

In terms of the human health hazard profiles for the 9 BFRs, it can be noted that the DNELs (general population, oral exposure) derived by the registrants were of different levels and the lowest among the substances was for TBP (2,4,6-TBP) (DNEL 0.25 mg/kg bw/day). This substance is on the CoRap list due to suspected CMR properties.

For skin sensitisation, two substances were positive for skin sensitisation and classified as Skin Sens. 1 (H317) (TBP (2,4,6-TBP) and (TEBP-Anh). Data on skin sensitisation were not available for the BFRs HEEHP-TEBP and EBTEBPI.

Different levels of data on *in vitro/in vivo* mutagenicity were available for the 9 BFRs, none of them fulfilling the test requirements for the highest tonnage level under REACH. Some indications for mutagenic activity were seen for most of the BFRs. Exceptions to this were TBNPP, HEEHP-TEBP, EBTEBPI and TTBP-TAZ, but test data were not adequate for a full evaluation. For DBNPG, data from a two-year combined chronic toxicity/carcinogenicity study (OECD 453) showed clear carcinogenic effects and the registrant has classified the substance as Carc. 2 (H351). For the other BFRs, data on carcinogenicity were not available. For HEEHP-TEBP the evaluation of carcinogenicity made by the registrant was based on read-across to data on phthalic anhydride (CAS 85-44-6-9).

Data on repeated dose toxicity studies are limited; mostly data from screening studies (OECD 421/422) and 28/90d studies (OECD 407/408) are available and none from chronic toxicity studies (two-year combined chronic toxicity/carcinogenicity study (OECD 453), except for DBNPG. For HEEHP-TEBP, the evaluations of repeated dose toxicity (inhalation and dermal) and developmental toxicity were by the registrant based on read-across to data on tetrabromophthalic anhydride (CAS 632-79-1). Specifically, for repeated dose toxicity (oral) the registrant used read-across to BEH-TEBP (BEHTBP) (CAS 26040-51-7).

In terms of data specifically related to endocrine activity, no data are available for the 9 BFRs. The available data from screening studies (OECD 421/422), repeated dose toxicity studies (OECD 407/408) and reproduction studies, do not specifically refer to possible endocrine activity. Specific endocrine endpoints investigating the underlying mechanism of

all types of endocrine disrupting effects would be anogenital distance and nipple retention, i.e. an antiandrogen effect, results from the Uterotrophic assay indicative of an oestrogen activity and further hormonal data (TSH, T3, T4), gene expression analysis representing major pathways of male reproduction tract development, and data on the thyroid.

For most of the BFRs data allowing evaluation of reproductive toxicity, endocrine activity and for some also developmental toxicity are lacking. For TBP (2,4,6-TBP), this BFR are on the CoRap-list based on suspected CMR properties. TTBP-TAZ is being evaluated in relation to a Risk Management Option Analysis (RMOA) based on suspected PBT properties. For three of the BFRs, TTBP-TAZ, BEH-TEBP (BEHTBP) and 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated testing is proposed by the registrant i.e. TTBP-TAZ: Two-generation reproduction study and a developmental toxicity study; BEH-TEBP (BEHTBP): A developmental toxicity study; 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated: Two-generation reproduction study and a developmental toxicity study.

Regarding the environmental fate and ecotoxicity of the substances, none of the substances are ready biodegradable under aerobic conditions. For HEEHP-TEBP only QSAR calculations were available for this endpoint.

Data on the acute toxicity towards aquatic organisms are generally available for all the substances. However, data for HEEHP-TEBP and TEBP-Anh are not available and are therefore based on QSAR calculations, except the endpoint acute toxicity to fish which is available for TEBP-Anh. For EBTEBPI, only acute toxicity data are available for fish. Long term toxicity studies are available for all the substances, except for HEEHP-TEBP and TEBP-Anh where only QSAR calculations are available, but generally lacking for fish.

Terrestrial data are generally lacking for all substances. For TBP data on the terrestrial toxicity are available for soil macroorganisms only and for TTBNPP data are available for both soil macroorganisms and plants.

None of the substances are considered to be PBT/vPvB substances by the registrants; a CORAP is available where TBP (2,4,6-TBP) is reported as a *suspected* PBT substance. For TTBP-TAZ, an RMOA is being performed at the moment based on *suspected* PBT properties.

#### **4.2 Conclusions in relation to substance evaluation**

With regard to priority for further evaluation the following conclusions were drawn for the BFRs, using the below described criteria for prioritisation. (High tonnage levels indicating a higher potential for exposure may further add to concern).

*Low level priority:* although data gaps occur, the available data do not indicate specific concern for some of the critical endpoints (CMR and PBT or endocrine disruption).

*Medium Level:* large data gaps are identified for hazard evaluation of critical endpoints (CMR and PBT or endocrine disruption), and the preliminary evaluation of concern is non-conclusive.

*High level:* available data indicate concern for some of the critical endpoints (CMR and PBT or endocrine disruption) and further evaluation is needed (and/or testing is needed in order to clarify the indicated concern).

The BFRs indicated with the highest priority may be recommended for further substance evaluation. For these substances justification documents ("Justification document for the selection of a CoRAP<sup>6</sup> substance") for suggested further substance evaluation will be filled out.

As indicated below a total of 3 BFRs was prioritized for further substance evaluation: HEEHP-TEBP (CAS: 20566-35-2), BEH-TEBP (BEHTBP) (CAS: 26040-51-7) and DBNPG (CAS: 3296-90-0)

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<sup>6</sup> Community rolling action plan

Short conclusions on the pre-screened BFRs:

**TBP (2,4,6-TBP) (CAS: 118-79-6):** The substance is already on the CoRAP-list as suspect CMR and PBT properties. Thus at this moment the substance is already considered a candidate of substance evaluation. Large data gaps are identified. Further, the registrant concludes that the substance is not a PBT substance. However, due to lack of data, P cannot be assessed based on the PBT criteria. TBP does not fulfil the screening criteria for B and T. A tonnage band up to 10000 tonnes/y is indicated.

Conclusion: *Low priority as the substance is already on CoRAP-list.*

**TTBNPP (19186-97-1):** Data are lacking on carcinogenicity, and mutagenicity is not fully examined. The available data on reproductive and developmental toxicity do not indicate any specific concern, however no two-generation reproduction study is available (or alternatively an extended one-generation reproduction study). The registrant concludes that the substance is not a PBT substance. However, in relation to PBT criteria, TBNPP does fulfil the screening criteria for P (not readily biodegradable) but not the criteria for B and T. The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *Low priority.*

**HEEHP-TEBP (CAS: 20566-35-2):** Very few data are available on the substance. Read-across is used in the registration dossier. Data on reproductive and developmental toxicity are lacking. The data set is very slim and the read-across should be further evaluated. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT, HEEHP-TEBP does not fulfil the screening criteria for P (however only QSAR), B (only calculated value) and T. Based on the structural resemblance to DEHP and the lack of data on reproductive and developmental toxicity, a need for further evaluation is indicated.

The tonnage band is indicated to be up to 100 tonnes/y.

Conclusion: *High priority.*

**TTBP-TAZ (CAS: 25713-60-4):** Data on CMR properties is limited, however a two-generation reproduction study and a developmental toxicity study are proposed by the registrant. A 90D study does not give reason to specific alert for carcinogenicity and reproductive toxicity. The registrant concludes that the substance is not a PBT substance. However, it is not readily biodegradable (screening criteria for P, vP fulfilled) and QSAR calculations indicate a potential for bioaccumulation (Log Kow > 4.5). Therefore, B and vB potential needs to be further evaluated. An RMOA is being performed at the moment based on *suspected* PBT properties. The tonnage band is indicated to be up to 10000 tonnes/y. The registration does not fulfil the data requirements for an Annex X registration but testing is proposed by registrant.

Conclusion: *Low priority based on an ongoing RMOA.*

**BEH-TEBP (BEHTBP) (CAS: 26040-51-7):** Large data gaps in the registration, Data on CMR properties are limited. Some alert (mutagenicity) could be raised from the available from in vitro testing. A developmental toxicity study is proposed by the registrant.. A concern could be raised due to the structural resemblance with DEHP. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT screening criteria, BEH-TEBP does fulfil the screening criteria for P but not B and T. Data on accumulation in biota does, however, indicate a bioaccumulation potential.

The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *high priority*

**EBTEBPI (CAS: 32588-76-4):** Data on CMR properties are limited g, however there is no indication of concern in the available data on developmental and repeated dose toxicity (90d). The registrant concludes that the substance is not a PBT. However, in relation to PBT screening criteria, EBTEBPI does fulfil the screening criteria for P (not ready biodegradable) but not B and T. The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *Low priority*

**DBNPG (CAS: 3296-90-0):** The available data on CMR endpoints indicate a concern for carcinogenic and mutagenic effects as well as possible toxicity to reproduction. Data are available from *in vitro* and *in vivo* studies showing that DBNPG is genotoxic with multi-site carcinogenic activity. Registrant has (only) classified as Carc. 2..

The registrant concludes that the substance is not a PBT substance. However, in relation to PBT criteria, DBNPG does fulfil the screening criteria for P (not ready biodegradable and inherently biodegradability is < 70%) and T (maybe fulfilled if classified as Carc. 1b.) but not B.

The tonnage band is indicated to be up to 1000 tonnes/y.

Conclusion: *high priority*

**TEBP-Anh (CAS: 632-79-1):** Very few data are available on the substance and read-across is used widely in the registration dossier. In general, data are lacking on reproductive and developmental toxicity. A concern for organ toxicity is noted from a repeated dose toxicity study. The data set is sparse and the justification for the applied read-across should be further evaluated. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT screening criteria, TEBP-Anh does fulfil the screening criteria for P (not ready biodegradable) but not B and T. The tonnage band is indicated to be up to 100 tonnes.

Conclusion: *Medium*

**2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS: 68441-62-3):** Data on CMR properties are limited and there are some indications on mutagenic activity based on *in vitro* assays, however *in vivo* data are negative. The registrant proposes to carry out a two-generation reproduction study and a developmental toxicity study. The registrant concludes that the substance is not a PBT substance. However, in relation to PBT screening criteria, 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated does fulfil the screening criteria for P (not ready biodegradable) but not B and T. The tonnage band is indicated to be up to 10 000 tonnes. The substance should be re-evaluated when testing has been performed.

Conclusion: *Low/medium priority*

It should be noted that for none of the substances there were data or discussion of possible endocrine disrupting properties or on combination effects with similar substances. However, indicative findings on 2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS 68441-62-3) suggests effects on sperm morphology. It is noted that the data were from a short-term repeated dose toxicity study.

*Overall conclusion:*

TBP (2,4,6-TBP) (CAS: 118-79-6) and TTBP-TAZ (CAS: 25713-60-4) are given low level prioritization due to on-going REACH activities (RMOA and CoRAP-list).

TTBNPP (19186-97-1) and EBTEBPI (CAS: 32588-76-4) are given low level prioritization due to no serious alert from existing data. Data gaps identified.

2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated (CAS: 68441-62-3) is given low/medium level prioritization due to on-going REACH activities (testing proposed by registrant).

TEBP-Anh (CAS: 632-79-1) is given medium prioritization due to data-gaps (reproductive and developmental toxicity), a concern for organ toxicity and the use of read-across. However, very low tonnage.

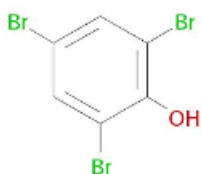
*And based on the current evaluation, HEEHP-TEBP (CAS: 20566-35-2), BEH-TEBP (BEHTBP) (CAS: 26040-51-7); DBNPG (CAS: 3296-90-0) are given high level prioritization and recommended for further evaluation.*

**Appendix 1: Data sheets for the 9 BRF's based on disseminated REACH registration dossier data available on the ECHA homepage. Data were extracted from October to November 2014. Key physical/chemical, toxicological and ecotoxicological endpoints are summarized.**

## TBP (2,4,6-TBP)

### Identification of substance

CAS No. 118-79-6  
EINECS No. 204-278-6  
IUPAC name 2,4,6-tribromophenol  
Structure



SMILES

### REACH

Registration Full  
Submission Joint Submission  
Total tonnage 1,000 - 10,000 tonnes per annum  
Harmonised classification Not classified  
Notified classification In total 108 notified classifications  
74 notifiers classify as:  
Skin Sens. 1 (H317)  
Eye Irrit. 2 (H319)  
Aquatic Acute 1 (H400)  
  
23 notifiers classify as:  
Acute Tox. 4 (H302)  
Skin Irrit. 2 (H315)  
Eye Irrit. 2 (H319)  
STOT SE 3 (H335)  
  
1 notifier classify as:  
Repr. 2 (H361)  
  
REACH registration classification Eye Irrit. 2 H319: Causes serious eye irritation.  
Skin Sens. 1 H317: May cause an allergic skin reaction.

### Physical-chemical characteristics

Molecular weight 330.8 g/mole (EpiSuite 4.1)  
Vapour pressure 0.063 Pa (25 °C) (EU Method A.4)



	Klimisch score: 1
Henry's law constant	-
Water solubility	50 mg/L (19 °C, pH: >6.9-<7) (OECD Guideline 105 (Water Solubility); EU Method A.6 (Water Solubility))
	Klimisch score: 1
Log K <sub>ow</sub>	Log Kow =3.7 (23.5 °C) (OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method); EU Method A.8 (Partition Coefficient))
	Klimisch score: 1

## Toxicological data

Sensitisation	<p>Skin sensitization (Guinea Pig Maximization Test -OECD 406)</p> <p>Positive skin responses 12/20 test animals (75% test compound)</p> <p>Positive skin responses 15/20 test animals (50% test compound)</p> <p>Severity ranged from 1 to 2 in all cases , 3 in one animal (50% test compound)</p> <p>Categorized as a strong sensitizer according to EU regulations</p> <p>Klimisch score: 1 (key study )</p>
Repeated toxicity	<p>NOAEL 50 mg/kg/day (local toxicity - forestomach squamous hyperplasia in the absence of other functional or morphological disturbances)</p> <p>NOAEL 150 mg/kg/day (systemic toxicity - increased albumin values and hepatocellular hypertrophy occurred in different sexes, were of a slight nature and were not indicative of clear functional disturbance. Therefore, these changes were considered to be adaptive rather than adverse)</p> <p>(28 day, oral, rat, 0, 50, 150, and 1000 mg/kg/day – OECD 407)</p> <p>(Klimisch score 1 (key study))</p> <p>NOEL 100 mg/kg/day (at 300 mg/kg/day, salivation and some changes in liver and kidney, including a high level of creatinine in the blood)</p> <p>(Combined repeated/reproduction study, rat, oral, 0, 30, 100, 300, 1000 mg/kg - OECD 422), (Klimisch score 2 (supporting study))</p> <p>NOEL 1000 mg/kg/day</p> <p>(28 day. Dermal, rabbit, 100, 300, and 1000 mg/kg – no guideline)</p> <p>(Klimisch score 2 (key study))</p>
Mutagenicity/genotoxicity	<p>Positive (clastogenic effects) in the vitro Mammalian Chromosome Aberration Test (+/- metabolic activation) (OECD Guideline 473)</p> <p>Klimisch score 1 (key study)</p> <p>Negative in vitro in the bacterial reverse mutation assay (+/- metabolic activation) - (OECD 471)</p> <p>Klimisch score 2 (weight of evidence - cross linking strain not included)</p> <p>Negative (not cytogenic) in the micronucleus chromosome aberration assay (OECD 474) - Klimisch score 1 (key study)</p> <p>Negative (not cytogenic) in the micronucleus chromosome aberration assay (OECD 474) - Klimisch score 1 (supporting study)</p>

Endocrine	No data
Carcinogenicity	No data
Reproductive and developmental toxicity	<p>Reproductive toxicity and developmental toxicity (OECD 422) – Combined repeated/reproduction screening study, rat, oral, 0, 30, 100, 300, 1000 mg/kg: NOAEL (reproduction) 1000 mg/kg/day (No effect on mean oestrous cycle, copulation, fertility, number of corpora lutea, implantation sites, number of pups born or live-born, the implantation index, or the delivery index) NOAEL (developmental) 300 mg/kg/day; LOAEL 1000 mg/kg/day (developmental/growth effect in pups and low number of live pups on Day 4 and viability index) (Klimisch score 2 (key study))</p> <p>Reproductive / developmental toxicity NOEL 300 mg/kg/day (at 1000 mg/kg/day, gestational / early post-partum parameters seen) (Combined repeated/reproduction study, rat, oral, 0, 30, 100, 300, 1000 mg/kg - OECD 422), (Klimisch score 2 (weight of evidence))</p> <p>NOEL 300 mg/kg/day (at 1000 mg/kg/day, increase in post-implantation loss and decrease in viable foetuses) (Pilot study, rat, oral, 0, 10, 30, 100, 300, 1000, and 3000 mg/kg daily from gestation day 6 to 15 - No guideline) (Klimisch score 2 (weight of evidence))</p>
Toxicokinetics/Metabolism	<p>A single oral gavage dose of between 4.0 and 5.3 mg/kg was rapidly absorbed and rapidly eliminated in rats of both genders. No tissue concentration The pharmacokinetics appears to follow a one-compartment model with first order kinetics. The half- life in tissues tested was between 1.45 and 2.3 hours, indicating no bioaccumulation or biopersistsens. (Klimisch score 2 (supporting study))</p> <p>A feeding study (1000 ppm for 7-21 days) in male rats showed increased fat residue after 7-days of feeding but no detectable amount of residue after a recovery period of 14-days or longer. (Klimisch score 2 (supporting study))</p>
DNEL (W) oral	No data
DNEL (W) inhalation	1.76 mg/m <sup>3</sup> (long-term)
DNEL (W) dermal	5.6 mg/kg bw/day (long-term)
DNEL (G) oral	0.25 mg/kg bw/day (long-term)
DNEL (G) inhalation	0.4 mg /kg bw/day (long-term)

DNEL (G) dermal	2.8 mg/kg bw/day (long-term)
On the CoRap list for further evaluation – the status is ongoing	Reason: Human health/CMR; Environment/Suspected PBT; Exposure/Wide dispersive use, high aggregated tonnage; Risk characterisation ratio close to 1 (environment)

## Ecotoxicological data

Algae	<p>EC<sub>50</sub> (<i>Pseudokirchnerella subcapitata</i>, 72 hours growth rate): 0.87 mg/L          NOEC (<i>Pseudokirchnerella subcapitata</i>, 72 hours growth rate): 0.1 mg/L          ISO 8692 (Water Quality - Fresh Water Algal Growth Inhibition Test with <i>Scenedesmus subspicatus</i> and <i>Selenastrum capricornutum</i>); OECD Guideline 201 (Alga, Growth Inhibition Test); EU Method C.3 (Algal Inhibition test))          Klimisch score: 1</p>
Crustaceans	<p>EC<sub>50</sub> (<i>Daphnia magna</i>, 48 hours): 0.26 mg/L          (OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test); EU Method C.2 (Acute Toxicity for Daphnia); ISO 6341 15 (Water quality - Determination of the Inhibition of the Mobility of <i>Daphnia magna</i> Straus (Cladocera, Crustacea)).          Klimisch score: 1</p> <p>NOEC (<i>Daphnia magna</i>, 21d) = 150 µg/L (reproduction) ((NOEC (21d) = 25 µg/L (mortality))          OECD Guideline 211 (Daphnia magna Reproduction Test)          Klimisch score: 1</p>
Fish	<p>LC<sub>50</sub> (<i>Cyprinus carpio</i>, 96 hours): 1 mg/L          (OECD 203, Acute Toxicity for Fish; EEC Directive 92/69 Part C.1)          Klimisch score: 1</p>
Terrestrial plants	-
Soil macroorganisms	<p>LC<sub>50</sub> (Earthworm, 14d) : 201 mg/kg soil dw          NOEC (Earthworm, 14d): 100 mg/kg soil dw          OECD Guideline 207 (Earthworm, Acute Toxicity Tests); EEC, Directive 87/302/EEC. Annex VIII of the EEC Directive 79/831/EEC, Toxicity for Earthworms. EEC Publication No. L 133; ISO 11268-1 (Effects of Pollutants on Earthworms. 1. Determination of Acute Toxicity Using Artificial Soil Substrate)          Klimisch score: 1</p>
PNEC (fresh water)	0.5 µg/L (Assessment factor: 50)
PNEC (marine water)	0.05 µg/L (Assessment factor: 500)
PNEC (fresh water sediment)	22.9 µg/kg sediment dw (partition coefficient)
PNEC (marine water sediment)	2.29 µg/kg sediment dw (partition coefficient)
PNEC (soil)	201 µg/kg soil dw (Assessment factor: 1000)

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## Environmental fate

Bioconcentration factor	BAF ( <i>Lepomis macrochirus</i> , 3d)= 20-140 (Published paper by Schultz DP 1973 J.Agr. Food Chem. 21:186.); (Published paper by Kuzeminiski SF, Brackett CK, Fisher JD 1975 J. Agr. Food Chem. 23:1060.); "most recent draft of the Guidelines for Registering Pesticides in the United States (January 30, 1978)" Klimisch score: 2
Ready biodegradability	Data reported however no results included
Adsorption/desorption	Koc: 2253 ml/g (OECD Guideline no 106) Klimisch score: 1

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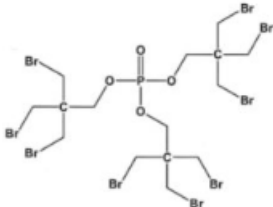
## PBT

REACH registration dossier -

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# TTBNPP

## Identification of substance

CAS No.	19186-97-1
EINECS No.	-
IUPAC name	Tri[3-bromo-2,2-bis(bromomethyl)propyl]phosphate
Structure	

## SMILES

## REACH

Registration	Three full registrations are available
Submission	They are all individual Submission
Total tonnage	1) 100 - 1,000 tonnes per annum 2) 1-10 tpa 3) 0-10 tpa
Harmonised classification	Not classified
Notified classification	Not classified
REACH registration classification	Not classified

## Physical-chemical characteristics

Molecular weight	- g/mole
Vapour pressure	$3 \cdot 10^{-13}$ Pa, 25 °C (Gas saturation method According to 84/449/EEC A.4) Klimisch score: 1
Henry's law constant	-
Water solubility	0.0156 mg/L (20 °C, pH 6.7) (OECD Guideline 105 (Water Solubility); EU Method A.6 (Water Solubility)) Klimisch score: 1
Log $K_{ow}$	4.87 (25°C, pH >6-<7) (OECD Guideline 123 (Partition Coefficient (1-Octanol / Water), Slow-Stirring Method)) Klimisch score: 2

## Toxicological data

Sensitisation	No skin sensitization (Guinea Pig Maximization Test -OECD 406) Klimisch score: 1 (key study)
Repeated toxicity	NOAEL 20000 ppm ( $\geq 1358 \leq 1658$ mg/kg bw/day (male/female) (90 day, oral (diet), rat, o, 2000, 10000, or 20000 ppm – OECD 408) (Klimisch score 1 (key study))

	NOAEL 20000 ppm ( $\geq 1361 \leq 2081$ mg/kg bw/day (male/female) (28 day, oral (diet), rat, o o, 4000, 8000, 20000 ppm – OECD 407) (Klimisch score 1 (key study))
Mutagenicity/genotoxicity	Negative in Bacterial Reverse Mutation Assay (+/- metabolic activation) (Test guideline described as 84-1; comparable to OECD 471?) - Klimisch score 1 (key study)  Negative in mammalian cell gene mutation assay (+/- metabolic activation) (forward mutations at the thymidine kinase (TK) locus in the mouse lymphoma L5178Y cell line) (Scientific reference, comparable to OECD476?) - Klimisch score 1 (key study)  Negative in the induction of structural aberrations in the <i>in vitro</i> mammalian cytogenetic assay using Chinese hamster ovary cells (+/- metabolic activation) Equivocal in the induction of numerical aberrations in the <i>in vitro</i> mammalian cytogenetic assay using Chinese hamster ovary cells (+/- metabolic activation) (EPA OPP 84-2) - Klimisch score 1 (key study)
Endocrine	No data
Carcinogenicity	No data
Reproductive and developmental toxicity	Reproductive toxicity and developmental toxicity screening: NOEC (Fo) > 2000 ppm (1590 mg/kg/day (male)/1775-4110 mg/kg/day (female) mg/kg/day) NOEC (F1) > 2000 ppm (3040 mg/kg/day (male)/3095 mg/kg/day (female) mg/kg/day) (No reproductive and developmental effects including timing of balano preputial separation for selected F1 males and of vaginal opening in F1 selected females) (2000, 10000 and 20000 ppm, oral (diet), rat – OECD 421) Klimisch score 1 (key study)  Developmental toxicity: NOAEL (maternal toxicity) 1000 mg/kg/day NOAEL (embryotoxicity) 300 mg/kg/day; LOAEL (embryotoxicity) 1000 mg/kg/day (slight reduction in fetal growth, no evidence of any adverse effects upon the mother nor any teratological effect upon development in utero) (100, 300 and 1000 mg/kg/day, oral(gavage), rat - OECD 414) Klimisch score 1 (key study)
Toxicokinetics/Metabolism	Single oral doses were administered to male and female albino rats at dose levels of 50 mg/kg (low dose) and 1000 mg/kg (high dose) with measuring of radioactivity to obtain information concerning the absorption, pharmacokinetics and rates and routes of excretion In addition, single oral doses were administered to male and female albino rats at a dose level of 50 mg/kg (low dose) and concentrations of radioactivity were measured in selected tissues and organs to obtain information concerning the distribution of the test compound. About 1% of dose was absorbed, hence no bioaccumulation potential.

	OECD 417) - Klimisch score 1 (Key study)
Other	No data
DNEL (W) oral	No data
DNEL (W) inhalation	95 mg/m <sup>3</sup> (long-term); 253.4 mg/m <sup>3</sup> (acute)
DNEL (W) dermal	13.6 mg/kg bw/day (long-term); 40 mg/kg bw/day (acute); 0.17 mg/cm <sup>2</sup> (long-term; local effects), 1 mg/cm <sup>2</sup> (acute; local effects),
DNEL (G) oral	6.79 mg/kg bw/day (long-term); 50 mg/kg bw/day (acute);
DNEL (G) inhalation	47.5 mg/m <sup>3</sup> (long-term); 126.7 mg/m <sup>3</sup> (acute)
DNEL (G) dermal	16.79 mg/kg bw/day (long-term); 20 mg/kg bw/day (acute) 0.17 mg/cm <sup>2</sup> (long-term; local effects), 0.5 mg/cm <sup>2</sup> (acute; local effects),
Classification proposed by registrant	Not classified

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## Ecotoxicological data

Algae	EC <sub>50</sub> ( <i>Pseudokirchnerella subcapitata</i> , 72 hours): > 100 mg/L (growth rate) NOEC ( <i>Pseudokirchnerella subcapitata</i> , 72 hours): > 100 mg/L (growth rate) (OECD Guideline 201 (Alga, Growth Inhibition Test)) Klimisch score: 1
Crustaceans	EC <sub>50</sub> ( <i>Daphnia magna</i> , 48 hours): >100 mg/L (OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)) Klimisch score: 1  NOEC ( <i>Daphnia magna</i> , 16 days): = 3.200 µg/L (reproduction) (OECD 202) Klimisch score: 1 <i>Note: the reported guideline OECD 202 is the "Daphnia sp. Acute Immobilisation Test". However the reported endpoint "reproduction" is a chronic endpoint (in the OECD Guideline no.211).</i>
Fish	LC <sub>50</sub> ( <i>Oncorhynchus Mykiss</i> , 96 hours): >100 mg/L (other guideline: Conform Annex V C3) Klimisch score: 1

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Terrestrial plants	NOEC (21d, <i>Allium cepa</i> ) < 0.1 mg/kg soil dw <i>Al.cepae;Av.satava;Be.vulgaris;Cu.sativus;Pi.sativum;Br.napus</i> OECD Guideline 208 (Terrestrial Plants Test: Seedling Emergence and Seedling Growth Test) (Multiple Dose Application) Klimisch score: 1
Soil macroorganisms	LC50 (14d, <i>Eisenia fetida</i> ) > 1000 mg/kg soil dw OECD Guideline 207 (Earthworm, Acute Toxicity Tests) ISO 11268-1 Klimisch score: 1
	NOEC (28d, <i>Eisenia fetida</i> ): 62.5 mg/kg soil dw OECD Guideline 222 (Earthworm Reproduction Test ( <i>Eisenia fetida</i> / <i>Eisenia andrei</i> )) Klimisch score: 1
PNEC (fresh water)	0.000312 mg/L (Assessment factor: 50)
PNEC (marine water)	0.00000312 mg/L (Assessment factor: 10)
PNEC (fresh water sediment)	1.45 mg/kg sediment dw (partition coefficient)
PNEC (marine water sediment)	0.145 mg/kg sediment dw (Assessment factor: 10)
PNEC (soil)	1 µg/kg soil dw (Assessment factor: 100)

## Environmental fate

Bioconcentration factor (BCF)	The BCF ( <i>Oncorhynchus mykiss</i> ) varies between less than 10 and 200 (EU Method C.13 (Bioconcentration: Flow-through fish test); OECD Guideline 305 (Bioconcentration: Flow-through Fish Test)) Klimisch score: 1
Ready biodegradability	Not readily biodegradable (39 d, 37%) EU Method C.4-C (Determination of the "Ready" Biodegradability - Carbon Dioxide Evolution Test) Modified Sturm test (7 days uptake/9days depuration) Klimisch score:1
Adsorption/desorption	log Koc: >5.63 (21°C)(OECD Guideline 121 (Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC))) Klimisch score: 1

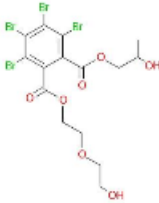
## PBT

REACH registration dossier -



# HEEHP-TEBP

## Identification of substance

CAS No.	20566-35-2
EINECS No.	243-885-0
IUPAC name	2-(2-hydroxyethoxy)ethyl 2-hydroxypropyl 3,4,5,6-tetrabromophthalate
Structure	

## SMILES

## REACH

Registration	Full
Submission	Joint submission
Total tonnage	10-100 tonnes per annum
Harmonised classification	Not classified
Notified classification	In total 95 notified classifications
	74: Aquatic Chronic 3 (H412)
	23: Not classified

## Physical-chemical characteristics

Molecular weight	627.91 g/mole (EpiSuite 4.1)
Vapour pressure	0 Pa (calculated) Klimish score:2
Henry's law constant	0 atm m <sup>3</sup> /mol (EPI Suite v3.20.1) Klimish score: 1
Water solubility	0.05697 mg/L (25°C) (Estimated) Klimish score:2
Log K <sub>ow</sub>	>3.8 (QSAR KOWWIN v1.68) Klimish score: 2

## Toxicological data

Sensitisation	No data
Repeated toxicity	Read-across from Di(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (DEHTBP/BEHTBP) [CASRN 26040-51-7] which is the brominated form of di(2-ethylhexyl)phthalate [CASRN 117-81-7]: NOAEL 2000 ppm (corresponding to approx. 223 mg/kg bw day)– Oral (Negative for peroxisome proliferation, a marker of PPAR $\alpha$ , di(2-

ethylhexyl)phthalate included as positive control)  
(28 day, rat, 0, 200, 2000, 20000 ppm in diet – OECD 407)  
Klimisch score 2 (key study)

Read-across from Tetrabromophthalic anhydride [CASRN 632-79-1] which is the brominated form of di(2-ethylhexyl)phthalate [CASRN 117-81-7]:  
NOEC 8 mg/L air – Inhalation  
(At 20 days hematological, biochemical, and urinalysis studies showed no change. Decreases in liver weights and increases in lung weights, however, were considered compound-related. The higher incidence of inflammatory lung lesions in both exposure groups compared to that in the control group may have also been compound-related. Necropsy showed no gross pathological lesions).  
(Dust exposures of 2 or 8 mg/L, 4 hr. daily, 5 d/wk., 3 wks., rat – no guideline)  
Klimisch score 2 (key study)

Read-across from Tetrabromophthalic anhydride [CASRN 632-79-1] which is the brominated form of di(2-ethylhexyl)phthalate [CASRN 117-81-7]:  
NOAEL 500 mg/kg bw/day - dermal  
LOAEL 5000 mg/kg bw/day (moderate erythema desquamation, death)  
(0, 50, 500, 5000 mg/kg, 5 d/wk., 4 wk, rabbit – No guideline)  
Klimisch score? (key study)

#### Mutagenicity/genotoxicity

Negative in Bacterial Reverse Mutation Assay (+/- metabolic activation)  
(no guideline but comparable to OECD 471 - 4 bacteria strains used)  
Klimisch score 1 (key study)

Negative in Bacterial Reverse Mutation Assay (+/- metabolic activation)  
(no guideline but comparable to OECD 471 - 4 bacteria strains and 1 yeast strain used) - Klimisch score 2 (weight of evidence)

#### Endocrine

No data

#### Carcinogenicity

Read-across from phthalic anhydride [CAS No. 85-44-9]:  
NOAEL (rats) 50000 ppm (male/female)  
NOAEL (mice) 12500 ppm (male/female)  
(Based on the histopathological examinations, no conclusive evidence for the carcinogenicity of phthalic anhydride in rats or mice was established. Further, no statistically or biologically significant changes in the reproductive organs of male rats or mice were found).  
(75000, 15000 ppm (rat); 25000, 50000 ppm (mice) in diet - EPA OPPTS 870.4200)  
Klimisch score 2 (key study)

#### Reproductive and developmental toxicity

Reproductive toxicity: No data

Developmental toxicity:  
Read-across from Tetrabromophthalic anhydride [CASRN 632-79-1] which is the brominated form of di(2-ethylhexyl)phthalate:  
NOEL (maternal toxicity) 3000 mg/kg  
(4 of 5 animals died at 10000 mg/kg)

(30 to 10000 mg/kg (0.065-21.565 mmol/kg), rabbit, oral (gavage) - OECD 414)  
Klimisch score 2 ( key study)

Toxicokinetics/Metabolism	No data
Other	Argumentation used for read-across approach in the REACH registration dossier: Studies with DEHTBP demonstrates that bromination of di(2-ethylhexyl)phthalate at the 3, 4, 5, and 6 position prevents the reproductive toxicity observed with di(2-ethylhexyl) phthalate in rodents. There are several possible explanations for this including: 1) DEHTBP may be poorly absorbed compared to di(2-ethylhexyl)phthalate; 2) if absorbed, DEHTBP or its metabolites may not act as an PPAR a agonists; or 3) if absorbed, DEHTBP may not cross the blood:testes barrier. Regardless, DEHTBP provides a worst case scenario of the potential for an esterified form of 3,4,5,6-tetrabromophthalic acid to induce reproductive toxicity. Bromination of a chemical shown to cause reproductive toxicity in rodents (i.e., di(2-ethylhexyl)phthalate) prevents that outcome. Because the reproductive toxicity of phthalate esters are associated with molecules that contain a 4 to 6 carbon linear or branched backbone, the absence of reproductive toxicity findings with DEHTBP, as well as, the absence of 4 to 6 carbon linear or branched aliphatic side chains in HEEHP-TEBP indicating that HEEHP-TEBP is not a candidate for inducing reproductive toxicity.
	No data
DNEL (W) oral	47 mg/m <sup>3</sup> (long-term); 0.43 mg/m <sup>3</sup> (acute)
DNEL (W) inhalation	47 mg/m <sup>3</sup> (long-term; local effects)
	89 mg/kg bw/day (long-term); 1600 mg/kg bw/day (acute);
DNEL (W) dermal	No data
DNEL (G) oral	No data
DNEL (G) inhalation	No data
DNEL (G) dermal	No data
	Not classified
Classification proposed by registrant	

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## Ecotoxicological data

Algae	EC <sub>50</sub> (96hours) = 4.391 mg/L (Q)SAR (ECOSAR)
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Crustaceans	LC50 (48h) = 9.927 mg/L (Q)SAR (ECOSAR) Klimish score: 2
	Chv: 1.266 mg/L (Q)SAR (ECOSAR) Klimish score: 2
Fish	LC50 (96 hours, <i>Lepomis macrochirus</i> ): 12 mg/L (Committee on methods for toxicity tests with aquatic organisms. 1975. Methods for acute toxicity tests with fish, macroinvertebrates and amphibians. EPA, Ecological Research Series EPA-660/3-75-009, April, 1975. 61 pp.) Klimish score 2:
	Chv: (32d): 0.447 mg/L (Q)SAR (ECOSAR) Klimish score: 2
Terrestrial plants	-
Soil macroorganisms	-
PNEC (fresh water)	0.011 mg/L (Assessment factor: 100)
PNEC (marine water)	-
PNEC (fresh water sediment)	No exposure of sediment expected
PNEC (marine water sediment)	-
PNEC (soil)	-

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### Environmental fate

Bioconcentration factor (BCF)	BCF: 390 (Estimation method (EPI Suite v3.20.)) Klimish score: 2
Ready biodegradability	Under test conditions no biodegradation observed (Estimated with BIOWIN v4.10) Klimish score: 2
Adsorption/desorption	Koc: 10 (Estimation method (EPI Suite PCKOCWIN v1.66)) Klimish score 2:

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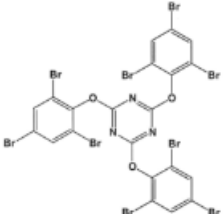
### PBT

REACH registration dossier	The substance is not PBT / vPvB
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# TTBP-TAZ

## Identification of substance

CAS No.	25713-60-4
EINECS No.	426-040-2
IUPAC name	2,4,6-Tris(2,4,6-tribromophenoxy)-1,3,5 triazine
Structure	

SMILES

## REACH

Registration	Full
Submission	Joint Submission
Total tonnage	1,000 - 10,000 tonnes per annum
Harmonised classification	Not classified
Notified classification	Not classified
REACH registration classification	Not classified

## Physical-chemical characteristics

Molecular weight	- g/mole
Vapour pressure	1.52*10 <sup>-20</sup> Pa (25°C) (OECD Guideline 104 (Vapour Pressure Curve); 92/69/EEC, A4 (Modified Watson Correlation method)) Klimisch score: 1
Henry's law constant	-
Water solubility	< 0.001 mg/L (20°C) (OECD Guideline 105 (Water Solubility); 92/69/EEC A6, (Column Elution method)) Klimisch score: 1
Log K <sub>ow</sub>	8.63 (average estimated value) (KOWWIN Program (v1.67)) Klimisch score: 2

## Toxicological data

Sensitisation	No skin sensitization potential (Guinea pig maximisation test-EU B.6.) - Klimisch score 1 (key study)
Repeated toxicity	<b>Oral</b> NOEL 1000 mg/kg bw/day (male/female) (highest dose level) (No effect on reproduction and Neurotoxicity: sperm count and motility, changes in the oestrus cycle, FOB analyses, histopathology) (0, 100, 350, 1000 mg/kg/day, oral (gavage), 90 day (+28 day recovery), rat –

OECD 408)  
Klimisch score 1 (key study)

NOEL 1000 mg/kg bw/day (male/female) (highest dose level)  
(No effect on reproduction and Neurotoxicity: sperm count and motility, changes in the oestrus cycle, FOB analyses, histopathology)  
(0, 100, 350, 1000 mg/kg/day, oral (gavage), 28 day, rat – Guideline in accordance with the "28-day Repeated Dose Toxicity study in Mammalian Species" prescribed in "Notification on Partial Revision of Testing Methods Relating to the New Chemical Substances" published in Notification No. 700 of the planning and Coordination)  
Klimisch score 1 (key study)

**Inhalation**

No data

**Dermal**

No data

Mutagenicity/genotoxicity Negative in *in vitro* Bacterial Reverse Mutation Assay (+/- metabolic activation) (OECD 471) - Klimisch score 1 (key study)

Negative in *in vitro* mammalian chromosome aberration test using peripheral human lymphocytes (+/- metabolic activation)  
(OECD 473) - Klimisch score 1 (key study)

Negative in mammalian cell gene mutation assay using mouse lymphoma L5178Y cells (TK locus) (+/- metabolic activation)  
(OECD 476) - Klimisch score 1 (key study)

Endocrine No data

Carcinogenicity No data

Reproductive and developmental toxicity Reproductive toxicity:  
No data. A testing proposal for a prenatal developmental toxicity study and a testing proposal for a 2-generation reproductive toxicity study has been included. Awaits feedback from ECHA.

Developmental toxicity:  
NOAEL (Maternal toxicity) 1000 mg/kg bw/day  
NOAEL (developmental toxicity) 1000 mg/kg bw/day  
(0, 250, 500, 1000 mg/kg bw/day, oral (gavage), rat - OECD 414)  
Klimisch score 1 (key study)

Toxicokinetics/Metabolism Toxicokinetics (rat - OECD 417):  
50 and 1000mg/kg/day of radiolabelled test article were administrated orally to rats. The absorption, distribution and excretion of the test article were studied up to 168 hours after administration. Very low absorption (<0.2%) of test article  
The majority of radioactivity was excreted in the faeces (main test article). Only

2.6% of the faecal extracts contained minor components, suggesting possible limited degeneration of the main test article.  
 No bioaccumulation potential based on study results.  
 Klimisch score 1 (key study)

Other	On data
DNEL (W) oral	No data
DNEL (W) inhalation	23.3 mg/m <sup>3</sup> (long-term); 50 mg/m <sup>3</sup> (acute) 23.3 mg/m <sup>3</sup> (long-term; local effects); 280 mg/m <sup>3</sup> (acute; local effects);
DNEL (W) dermal	3.3 mg/kg bw/day (long-term); 40 mg/kg bw/day (acute) 0.08 mg/cm <sup>2</sup> (long-term; local effects); 1 mg/cm <sup>2</sup> (acute; local effects);
DNEL (G) oral	1.7 mg/kg bw/day 12 mg/m <sup>3</sup> (long-term); 140 mg/m <sup>3</sup> (acute)
DNEL (G) inhalation	12 mg/m <sup>3</sup> (long-term; local effects); 140 mg/m <sup>3</sup> (acute; local effects);
DNEL (G) dermal	No data
Classification proposed by registrant	Not classified
PACT	This Public Activities Coordination Tool (PACT) lists the substances for which a Risk Management Option Analysis (RMOA) is either under development or has been completed since the implementation of the SVHC Roadmap commenced in February 2013.  Reason: PBT (decision development)

## Ecotoxicological data

Algae	EC <sub>50</sub> ( <i>Pseudokirchnerella subcapitata</i> , 72 hours): > 0.013 mg/L (growth rate) NOEC ( <i>Pseudokirchnerella subcapitata</i> , 72 hours): > 0.013 mg/L (growth rate) (other guideline: 92/69/EEC, C.3 OECD 201 (1989)) Klimisch score: 1
Crustaceans	EC <sub>50</sub> ( <i>Daphnia magna</i> , 48 hours): >0.013 mg/L (other guideline: 92/69/EEC, C.2 OECD 202 (1984)) Klimisch score: 1  -
Fish	LC <sub>50</sub> ( <i>Cyprinus carpio</i> , 96 hours): >0.013 mg/L (other guideline: 92/69/EEC, C.1 OECD 203 (1992)) Klimisch score: 1

Terrestrial plants	NOEC ( <i>Lycopersicon esculentum</i> , 21 days): >2.3 mg/kg soil dw (OECD Guideline 208 (Terrestrial Plants Test: Seedling Emergence and Seedling Growth Test)) Klimisch score: 1
Soil macroorganisms	EC50 ( <i>Eisenia fetida</i> , 28days): >1000 mg/kg soil dw (mortality and reproduction) NOEC ( <i>Eisenia fetida</i> , 28days): >1000 mg/kg soil dw (mortality and reproduction) (OECD Guideline 222 (Earthworm Reproduction Test (Eisenia fetida/Eisenia andrei))) Klimisch score: 1
PNEC (fresh water)	0.00001 mg/L (registration 2: 0.00037 mg/L)
PNEC (marine water)	0.000001 mg/L (registration 2: 0.000037 mg/L)
PNEC (fresh water sediment)	20 mg/kg sediment dw (assessment factor: 50)
PNEC (marine water sediment)	2 mg/kg sediment dw (assessment factor: 500)
PNEC (soil)	0.246 mg/kg soil dw (assessment factor: 50)

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## Environmental fate

Bioconcentration factor (BCF)	-
Ready biodegradability	Not inherently biodegradable (39d, 4%) (OECD Guideline 302 D (Inherent Biodegradability - Concawe Test)) Klimisch score: 1
Adsorption/desorption	log Koc: 9.53 (35 °C) (OECD Guideline 121 (Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC)); EU Method C.19 (Estimation of the Adsorption Coefficient (KOC) on Soil and Sewage Sludge Using High Performance Liquid Chromatography (HPLC))) Klimisch score: 1

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## PBT

REACH registration dossier	The substance is not PBT / vPvB
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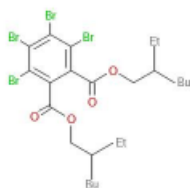


# BEH-TEBP (BEHTBP)

## Identification of substance

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CAS No.	26040-51-7
EINECS No.	247-426-5
IUPAC name	bis(2-ethylhexyl) tetrabromophthalate
Structure	



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### SMILES

## REACH

Registration	Full
Submission	Joint Submission
Total tonnage	100 – 1,000 tonnes per annum
Harmonised classification	Not classified
Notified classification	In total 24 notified classifications

22: Eye irrit. 2 (H319)

2: Not classified

REACH registration classification	Not classified
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## Physical-chemical characteristics

Molecular weight	706.15 g/mole (Epi-Suite v 4.1)
Vapour pressure	0.000000356 Pa (25 °C) (QSAR, modified Grain method) Klimisch score: 2
Henry's law constant	-
Water solubility	Insoluble (< 0.1 mg/L) The water solubility of the substance could not be detected without solubilizer and is reported to be < 0.05 µg/l. With 1% acetonitrile as solubilizer a water solubility of 794 µg/l could be detected. (OECD Guideline 105 (Water Solubility); EU Method A.6 (Water Solubility)) Klimisch score: 1
Log K <sub>ow</sub>	10.2 (25 °C, pH 6.1) (EU Method A.8 (Partition Coefficient))

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## Toxicological data

Sensitisation	No skin-sensitization potential (Guinea-pig test, modified version of the method of Buehler, no dermal response to occluded application at any of the induction phases, no significant dermal response to challenge application – OECD 406) Klimisch score 1 (key study)
Repeated toxicity	<b>Oral</b> NOAEL 2000 ppm (= ca. 223.4 mg/kg bw (male/female)) LOAEL 20000 ppm (lower body weight gain, alanine amino-transferase activities and phosphorus concentrations) (No liver and testes changes as seen in the positive control group DEHP, particularly in respect of peroxisome proliferation) (200, 2 000, 20 000 ppm (= ca. 21.97, 223.4, 2331 mg/kg/day), oral (diet), 28 day, rat – OECD 407) Klimisch score 1 (key study)  <b>Inhalation</b> No data  <b>Dermal</b> No data
Mutagenicity/genotoxicity	Positive in the <i>in vitro</i> Mammalian Chromosome Aberration Test using human lymphocytes (+/- metabolic activation) (Weak clastogenic activity (statistically significant increases in aberrant cell frequencies were seen both including and excluding gaps) at 1000 ug/ml) (OECD 473) - Klimisch score 1 (key study)  Negative in the <i>in vitro</i> Bacterial Reverse Mutation Assay using five histidine-dependent bacterial strains TA 98, TA 1538, TA 100, TA 1535 and TA 1537 (+/- metabolic activation) (OECD 471) - Klimisch score 1 (key study)  Negative in the <i>in vitro</i> in mammalian cell gene mutation assay using Chinese hamster lung fibroblasts (HPRT locus in V79 cells) - (+/- metabolic activation) (OECD 476) - Klimisch score 1 (key study)  Negative in the <i>in vivo</i> Mammalian Erythrocyte Micronucleus assay (chromosome structure in bone marrow cells was investigated following acute intraperitoneal (0, 250, 500, 1000, 2000 mg/kg bw) and sub-acute dermal (2000 mg/kg bw) administration to mice) (OECD 474) - Klimisch score 1 (key study)
Endocrine	No data
Carcinogenicity	No data

Reproductive and developmental toxicity	<p>Reproductive toxicity:  NOAEL 20000 ppm (ca. 2331 mg/kg bw) (male/female – P generation)  (The pathologic evaluation consisted of organ weight, gross and microscopic examination of reproductive organs, incl. epididymides, mammary glands - caudal, ovaries, prostate, testes, and uterus (with cervix). No organ weight changes and histopathological changes in reproductive organs (male/female)).  (200, 2 000, 20 000 ppm (ca. 21.97, 223.4, 2331 mg/kg/day), oral (diet), 28 day, rat – OECD 407 with examination of reproductive organs but no reproduction!)  Klimisch score 2 (key study)</p> <p>Developmental toxicity:  OECD 414 planned (testing proposal to ECHA – no information on status)</p>
Toxicokinetics/Metabolism	<p>The in vitro metabolism of bis(2-ethylhexyl)tetrabromophthalate was investigated in human and rat tissues (subcellular fractions of human liver/rat liver and intestinal tissues). No metabolites were detected in human or rat subcellular fractions. However, a metabolic product (mono(2-ethylhexyl)tetrabromophthalate (TBMEHP)), was formed in purified porcine carboxylesterase at an approximate rate of 1.08 pmol/ min/ mg protein. No phase II metabolites were observed.  Klimisch score 2 (supporting study)</p>
Other	<p>An in vitro approach was used to determine the concentration-dependent effects on overt toxicity and hepatic messenger RNA (mRNA) expression levels of 11 transcripts in primary cultures of chicken embryonic hepatocytes (CEH). Hepatocyte viability was not affected by bis(2-ethylhexyl)tetrabromophthalate at any of the administered concentrations (0.001–30µM). None of the gene targets were responsive to bis(2-ethylhexyl)tetrabromophthalate exposure in CEH.  Klimisch score 2 (supporting study)</p>
DNEL (W) oral	No data
DNEL (W) inhalation	5.25 mg/m <sup>3</sup> (long-term); 26.25 mg/m <sup>3</sup> (short-term)
DNEL (W) dermal	0.74 mg/kg bw/day (long-term); 3.7 mg/kg bw/day (short-term)
DNEL (G) oral	0.37 mg/kg bw/day (long-term)
DNEL (G) inhalation	1.29 mg/m <sup>3</sup> (long-term); 6.45 mg/m <sup>3</sup> (short-term)
DNEL (G) dermal	0.37 mg/kg bw/day (long-term); 1.85 mg/kg bw/day (short-term)
Proposed classification by registrant	No classification

## Ecotoxicological data

Algae	EC50 ( <i>Desmodesmus subspicatus</i> , 72 hours): >100 mg/L (growth rate)
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	EC10 ( <i>Desmodesmus subspicatus</i> , 72 hours): >100 mg/L (growth rate) (OECD Guideline 201 (Alga, Growth Inhibition Test); EU Method C.3 (Algal Inhibition test)) Klimisch score: 1
Crustaceans	EC50 ( <i>Daphnia magna</i> , 48 hours): >10 mg/L (OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test); EU Method C.2 (Acute Toxicity for Daphnia)) Klimisch score: 2
	NOEC ( <i>Daphnia magna</i> , 21 days): >= 1 mg/L (OECD Guideline 211 (Daphnia magna Reproduction Test); EU Method C.20 (Daphnia magna Reproduction Test)) Klimisch score: 1
Fish	LC50 ( <i>Oncorhynchus mykiss</i> , 96 hours): >1,000 mg/L (OECD Guideline 203 (Fish, Acute Toxicity Test)) Klimisch score: 2
	-
Terrestrial plants	-
Soil macroorganisms	-
PNEC (fresh water)	-
PNEC (marine water)	-
PNEC (fresh water sediment)	-
PNEC (marine water sediment)	-
PNEC (soil)	-

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## Environmental fate

Bioconcentration factor	BMF: 0.0012-0.014. (No guideline; The method is comparable to the OECD guideline 305. Test organism: Pimephales promelas, exposure: 56d, depuration: 22d)) Klimisch score: 2
Ready biodegradability	Not inherently biodegradable (7%, 28d) (OECD Guideline 302 C (Inherent Biodegradability: Modified MITI Test (II))) Klimisch score: 1
Adsorption/desorption	log Koc: 7.3 (25 °C) (EU Method C.19 (Estimation of the Adsorption Coefficient (KOC) on Soil and Sewage Sludge Using High Performance Liquid Chromatography (HPLC))) Klimisch score: 1

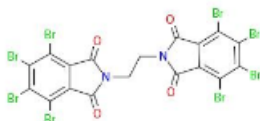
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## PBT

# EBTEBPI

## Identification of substance

CAS No.	32588-76-4
EINECS No.	251-118-6
IUPAC name	2,2'-ethane-1,2-diylbis(4,5,6,7-tetrabromo-1H-isoindole-1,3(2H)-dione)
Structure	



### SMILES

## REACH

Registration	Full
Submission	Joint Submission
Total tonnage	100-1,000 tonnes per annum
Harmonised classification	Not classified
Notified classification	In total 83 notified classifications
	63: No information
	20: Not classified
REACH registration classification	Not classified

## Physical-chemical characteristics

Molecular weight	951.47 g/mole (Epi-suite v4.1)
Vapour pressure	0.000227 Pa (20 °C)(EPA OPPTS 830.7950 (Vapour Pressure); OECD Guideline 104 (Vapour Pressure Curve))
	Klimisch score: 1
Henry's law constant	0 Pa m <sup>3</sup> /mol, 25 °C (calculated)
	Klimisch score: -
Water solubility	< 1 mg/L, ambient air temperature (no guideline followed)
	Klimisch score: -
Log K <sub>ow</sub>	-

## Toxicological data

Sensitisation	No data (study scientifically unjustified, references included but not used)
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Repeated toxicity	<p><b>Oral</b>  NOEL 1% (approximately 1000 mg/kg/bw)  (28 day, rat, 0, 0.01, 0.1 and 1% in diet - OECD 407)  Klimisch score 2 (key study) (performed prior to international guidelines/GLP)</p> <p>NOEL 1% (approximately 1000 mg/kg/bw)  (90 day, rat, 0, 0.01, 0.1 and 1% in diet - OECD 408)  Klimisch score 2 (key study) (performed prior to international guidelines/GLP)</p> <p><b>Inhalation</b>  No data</p> <p><b>Dermal</b>  No data</p>
Mutagenicity/genotoxicity	<p>Negative in <i>in vitro</i> Bacterial Reverse Mutation Assay (+/- metabolic activation) (Japan: Guidelines for Screening Mutagenicity Testing Of Chemicals) - Klimisch score 1 (key study)</p> <p>Negative in <i>in vitro</i> mammalian chromosome aberration test using CHO cells (+/- metabolic activation) (OECD 473) - Klimisch score 1 (key study)</p>
Endocrine	No data
Carcinogenicity	No data
Reproductive and developmental toxicity	<p>Reproductive toxicity: No data</p> <p>Developmental toxicity:  NOEL (maternal toxicity) 1000 mg/kg bw/d  NOEL (embryotoxicity/foetotoxicity) 1000 mg/kg bw/d  (No maternal, embryo or fetal toxicity or malformations at doses up to 1000 mg/kg/d from GD 7-19)  (0, 1000 mg/kg bw/d, Rabbit, Oral (gavage) - EPA OPPTS 870.3700 (Prenatal Developmental Toxicity Study))  Klimisch score 1 (key study)</p> <p>NOEL (maternal toxicity) 1000 mg/kg bw/d  NOEL (embryotoxicity/foetotoxicity) 1000 mg/kg bw/d  (No maternal, embryo or fetal toxicity or malformations at doses up to 1000 mg/kg/d from GD 6-15)  (0, 1000 mg/kg bw/d, Rat, Oral (gavage) - EPA OPPTS 870.3700 (Prenatal Developmental Toxicity Study))  Klimisch score 1 (key study)</p>
Toxicokinetics/Metabolism	<p>Toxicokinetics (rat – no guideline):  Radioactive labelled test article (~0.67 mg/kg) administered to 5 female rats by gavage for 14 consecutive days was excreted primarily in the feces (65%) and urine (15%) during exposure period. At the end of dosing, the tissues with the</p>

highest<sup>14</sup>C-activity were liver (~0.39 ppm) and kidney (~0.32 ppm). Levels in both dropped rapidly (by ~50%) during the first 7 days of withdrawal, and continued to drop over the withdrawal period. Levels in muscle (~0.08 ppm), fat (~0.075 ppm) and brain (~0.032 ppm) were substantially below that of the liver and kidney after 14 days of dosing. By day 14 of the withdrawal period, no<sup>14</sup>C-activity was detected in fat. <sup>14</sup>C-activity in the liver, kidney, muscle and brain continued to fall between 14 and 30 days of withdrawal, and were below 0.05 ppm by 30 days post-treatment. The highest level at 30 day post-treatment was found in the skeletal muscle (0.05 ppm). Hence, a low bioaccumulation potential. Klimisch score 2 (key study).

Other No data (no hazard identified)

No data

DNEL (W) oral

No data

DNEL (W) inhalation

No data

DNEL (W) dermal

No data

DNEL (G) oral

No data

DNEL (G) inhalation

No data

DNEL (G) dermal

Classification proposed by registrant

Not classified

## Ecotoxicological data

Algae

-

Crustaceans

-

-

Fish

LC<sub>50</sub> (*Oryzias latipes*, 48 hours): >500 mg/L

(other guideline: In accordance with the "Law Concerning the Examination and Regulation of Manufacture, etc., of Chemical Substances" (Japn 1973. Law No. 117))

Klimisch score: 1

-

Terrestrial plants

-

Soil macroorganisms	-
PNEC (fresh water)	-
PNEC (marine water)	-
PNEC (fresh water sediment)	-
PNEC (marine water sediment)	-
PNEC (soil)	-

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### Environmental fate

Bioconcentration factor (BCF)	0.3-3.3 (8 weeks exposure, no depuration, <i>Cyprinus carpio</i> ) (other guideline: In accordance with the "Law Concerning the Examination and Regulation of Manufacture, etc., of Chemical Substances" (Japan 1973. Law No. 117)) Klimisch score: 2
Ready biodegradability	Not readily biodegradable (0%, 14d) (other guideline: In accordance with the "Law Concerning the Examination and Regulation of Manufacture, etc., of Chemical Substances (Japan. 1973. Law No. 117.)) Klimisch score: 1
Adsorption/desorption	Koc: 690,000 (estimated by calculation from Log Kow) Klimisch score: 2

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### PBT

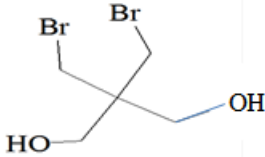
REACH registration dossier QSAR	The substance is not PBT / vPvB -
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# DBNPG

## Identification of substance

CAS No.	3296-90-0
EINECS No.	221-967-7
IUPAC name	2,2-bis(bromomethyl)propane-1,3-diol
Structure	

## SMILES

## REACH

Registration	Full
Submission	Individual Submission
Total tonnage	100-1,000 tonnes per annum
Harmonised classification	Not classified
Notified classification	In total 472 notified classifications

*355 notifiers classify as:*

Acute Tox. 4 (H302)

Eye Irrit. 2 (H319)

Muta. 2 (H341)

*81 notifiers classify as:*

Eye Irrit. 2 (H319)

Muta. 1B (H340)

Carc. 1B (H350)

STOT RE 2 (H373)

Aquatic Chronic 4 (H413)

REACH registration classification	Carc. 2 H351: Suspected of causing cancer Route of exposure: Oral
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## Physical-chemical characteristics

Molecular weight	261.94 g/mole (Epi-Suite v4.1)
Vapour pressure	$2 \cdot 10^{-3}$ Pa (25 °C) (OECD Guideline 104 (Vapour Pressure Curve)) Klimisch score: 1
Henry's law constant	-
Water solubility	19.4 g/L (20±0.5°C) (OECD Guideline 105 (Water Solubility) Method 830.7840)

of the OPPTS Guidelines)

Klimisch score: 1

Log K<sub>ow</sub>

1.08 (OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method) Method 830.7570 of the OPPTS Guidelines)

Klimisch score: 1

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## Toxicological data

Sensitisation

No skin sensitisation (Guinea pig maximisation test - OECD 406)  
(No skin reactions at challenge sites after 24/48h using 50% and 75 w/w)  
Klimisch score 1 (Key study)

Repeated toxicity

### Oral

LOAEL (13 wk. rat) 2500 ppm (400 mg/bw/day)

LOAEL (13 wk. mice) 312 ppm (35 mg/bw/day)

(Rat: 0, 1250, 2500, 5000, 10000, 20000 ppm; Mice: 0, 625, 1250, 2500, 5000 ppm corresponding to Rat: 95, 185, 400, 800, 1700 mg/bw/day for males and 100, 200, 400, 800, 1630 mg/kg (females); Mice: 100, 200, 480, 1285, 2930 mg/kg (males) and 140, 300, 640, 1180, 2900 mg/kg (females); diet – OECD 453 (Combined Chronic Toxicity / Carcinogenicity Study but no neurological nor ocular assessments included).

Klimisch score 1 (Key study)

13 wk. toxicity studies (5d/wk.) to determine target organ toxicity, orally (by gavage or feed), rats and mice, to determine target organ toxicity. Rats: 0, 50, 100, 200, 400, and 800 mg/kg; Mice: 0, 25, 50, 100, 200, and 400 mg/kg, or in the feed for 13 weeks at 0, 1250, 2500, 5000, 10,000, and 20,000 ppm. Minimal generation in the renal papilla was seen in male rats at 800 mg/kg in the gavage study and at doses of 5000 ppm or more in the feed study. This was also present in one female rat at the 20,000 ppm dose. In male mice renal papillary necrosis occurred at 400 mg/kg and at 2500, 5000 and 10,000. In female mice papillary necrosis occurred only in the 10,000 ppm. Tubular cell regeneration of the renal cortex was also present in mice at the same dose levels at which the papillary necrosis was observed. Transitional cell hyperplasia of the urinary bladder was seen in male rats at 400 mg/kg and in both sexes of mice 200 and 400 mg/kg. The kidney and urinary bladder were the target organs. Mice were more sensitive than rats for the development of kidney and bladder lesions. Male rats and mice were more sensitive than females for the development of renal papillary degeneration or necrosis. No NOAEL/LOAEL derived. Klimisch score 2 (Supporting study)

### Inhalation

No data

### Dermal

No data

Mutagenicity/genotoxicity

Positive in vitro in Bacterial Reverse Mutation Assay

(TA1535 and TA100; + metabolic activation – hamster S9 mix))

Negative in vitro in Bacterial Reverse Mutation Assay

(TA 1535, TA 1537, TA 98 and TA 100 +/- metabolic activation – rat S9 mix)

(OECD 471) - Klimisch score 1 (Key study)

Equivocal in vitro in mammalian cell gene mutation assay in CHO cells.  
(Negative in sister chromatid exchanges (- metabolic activation))  
(Positive, very slight increases in sister chromatid exchanges at toxic levels (+ metabolic activation))

(OECD 476) - Klimisch score 2 (Key study) EU Method B.19 (Sister Chromatid Exchange Assay In Vitro)

Positive in vitro in mammalian chromosome aberration test using Chinese hamster ovary cells (+ metabolic activation)

Negative in vitro in mammalian chromosome aberration test using Chinese hamster ovary cells (- metabolic activation)

(No guideline) - Klimisch score 2 (supporting study)

Endocrine

No data

Carcinogenicity

LOAEL 2500 ppm (male/female rat)

LOAEL 312 ppm (male/female mice)

(Rat: 0, 1250, 2500, 5000, 10000, 20000 ppm; Mice: 0, 625, 1250, 2500, 5000 ppm corresponding to Rat: 95, 185, 400, 800, 1700 mg/bw/day for males and 100, 200, 400, 800, 1630 mg/kg (females); Mice: 100,200,480, 1285, 2930 mg/kg (males) and 140, 300,640, 1180,2900mg/kg (females); diet – OECD 453 (Combined Chronic Toxicity / Carcinogenicity Study but no neurological nor ocular assessments included)

Klimisch score 2 (Key study )

Rats: In male rats, exposure was associated with neoplastic effects in the skin, mammary, gland, and Zymbal's gland, oral cavity esophagus, forestomach, small and large intestines, mesothelium, urinary bladder, lung, thyroid gland hematopoietic system, and seminal vesicle. Non neoplastic effects in the kidney, lung, thyroid gland, seminal vesicle, pancreas, urinary bladder, and forestomach were also observed. In female rats, increased incidences of neoplasms of the oral cavity, esophagus, mammary gland and thyroid gland was observed.

Mice: In male mice increased incidences of neoplasms of the Hadrian gland, lung and kidney was observed. In female mice increased incidences of neoplasms of the Hadrian gland, lung and subcutaneous tissue was observed. Slight increases in the incidences of neoplasms in the pancreas and kidney in male mice and the forestomach, mammary gland and circulatory system in female mice may also have been related to treatment.

Reproductive and developmental toxicity

Reproductive toxicity:

NOEL 0.1 % w/w (P, F1, F2)

(The 0.4% dose level adversely affected reproduction in CD1 mice. Continued treatment at this dose level also resulted in a significant drop in body weight. The crossover mating study showed that it was the reproductive performance of female mice that was affected by treatment with the substance at the 0.4% dose level. The number of live pups per litter delivered by the 0.4% female x control male group being significantly lowers than the 0.4% male x control female group.

The reproductive performance of second generation CD-1 mice exposed to the substance at the 0.4% dose level was adversely affected with respect to the number of live pups per litter and the adjusted live pup weight. Second generation animals in the 0.4% group weighed less than the control group at weaning, through maturation and at necropsy.

(Two generations reproduction study, 0, 0.1, 0.2, 0.4 % w/w, mice – No guideline -The study was performed using the NTP Fertility Assessment by Continuous Breeding (FACB) system. It consists of four related tasks as follows: 1. dose finding. 2. Continuous breeding phase. 3. Identification of the affected sex. 4 offspring assessment)  
Klimisch score 1 (Key study)

Developmental toxicity:  
No data

Toxicokinetics/Metabolism	<p>The toxicokinetics was explored after a single oral or intravenous administration of radioactive test substance to male F-344 rats. Additional studies were designed to determine whether repeated oral administration (5 or 10 days) alters its disposition profile. The test data indicate that the extensive extraction and rapid glucuronidation (metabolites) by the liver limits exposure of internal tissues by greatly reducing its systemic bioavailability after oral exposure.</p> <p><u>Absorption:</u> After a single oral administration (10 or 100 mg/kg) &gt;80% of the low dose and 48% of the high dose were excreted by 12 h in the urine.</p> <p><u>Distribution:</u> the total percentage of radioactivity remaining in tissues at 72h after was less than 1%. Adipose tissues, liver, kidneys, muscle, and skin contained 0.2, 0.7, 0.1, 0.3, and 0.3% of dose, respectively.</p> <p><u>Metabolism:</u> glucuronidation metabolite</p> <p><u>Excretion:</u> After a single oral administration (10 or 100 mg/kg) &gt;80% of the low dose and 48% of the high dose were excreted by 12 h in the urine. Hence, low bioaccumulation potential based on study results. (No guideline followed but similar/equivalent to OECD 417) Klimisch score 1 (Key study)</p>
Other	No data
DNEL (W) oral	No data
DNEL (W) inhalation	No data
DNEL (W) dermal	100 mg/kg bw/day (long-term); 1.4 mg/cm <sup>2</sup> (acute)
DNEL (G) oral	No data
DNEL (G) inhalation	No data
DNEL (G) dermal	No data
Proposed classification by registrant	Carc. 2 H351: Suspected of causing cancer Route of exposure: Oral

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## Ecotoxicological data

Algae	EC <sub>50</sub> ( <i>Desmodesmus subspicatus</i> , 72 hours): 37 mg/L NOEC ( <i>Desmodesmus subspicatus</i> , 72 hours): 12.5 mg/L (OECD Guideline 201 (Alga, Growth Inhibition Test)) Klimisch score: 1
Crustaceans	EC <sub>50</sub> ( <i>Daphnia magna</i> , 48 hours): >100 mg/L (OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)) Klimisch score: 1
Fish	LC <sub>50</sub> ( <i>Oncorhynchus mykiss</i> , 96 hours): >100 mg/L (OECD Guideline 203 (Fish, Acute Toxicity Test)) Klimisch score: 1
Terrestrial plants	-
Soil macroorganisms	LC <sub>50</sub> ( <i>Eisenia fetida</i> , 14 days): 540 mg/kg NOEC ( <i>Eisenia fetida</i> , 14 days): 180 mg/kg (OECD Guideline 207 (Earthworm, Acute Toxicity Tests)) Klimisch score: 1
PNEC (fresh water)	0.037 mg/L (Assessment factor: 1000)
PNEC (marine water)	0.0037 mg/L (Assessment factor: 10000)
PNEC (fresh water sediment)	0.0371 mg/kg sediment dw (partition coefficient)
PNEC (marine water sediment)	0.00371 mg/kg sediment dw (partition coefficient)
PNEC (soil)	0.54 mg/kg soil dw (Assessment factor: 1000)

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## Environmental fate

Bioconcentration factor (BCF)	1.1 (MITI; <i>Cyprinus carpio</i> ) Klimisch score: 2 <4.8 (MITI; <i>Cyprinus carpio</i> ) Klimisch score: 2
Ready biodegradability	Not readily biodegradable (25%, 28d) (OECD Guideline 301 B (Ready Biodegradability: CO <sub>2</sub> Evolution Test) OPPTS 835.3110) Klimisch score: 1

Inherently biodegradable (44%, 33d)  
OECD Guideline 302 D (Inherent Biodegradability - Concawe Test) OECD  
Guideline 302B (Inherent Biodegradability: Zahn-Wellens/EMPA Test  
Klimish score 2  
Adsorption/desorption log Koc: <1.25 (OECD Guideline 121 (Estimation of the Adsorption Coefficient  
(Koc) on Soil and on Sewage Sludge using High Performance Liquid  
Chromatography (HPLC)))  
Klimisch score: 1

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## PBT

REACH registration dossier -

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# TEBP-Anh

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CAS No.	632-79-1
EINECS No.	211-185-4
IUPAC name	4,5,6,7-tetrabromo-2-benzofuran-1,3-dione
Structure	



SMILES

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## REACH

Registration	Full
Submission	Joint Submission
Total tonnage	10 - 100 tonnes per annum
Harmonised classification	Not classified
Notified classification	In total 424 notified classifications <i>355 notifiers classify as:</i> Not classified <i>42 notifiers classify as Skin Sens. 1 (H317)</i>
REACH registration classification	Not classified

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## Physical-chemical characteristics

Molecular weight	463.7 g/mole (Epi-Suite v.4.1)
Vapour pressure	ca. 0.00000273 Pa (EPI v 3.20) Klimisch score: 1
Henry's law constant	0.016 Pa m <sup>3</sup> /mol (EPI Suite™ v3.20) Klimisch score: 2
Water solubility	241 mg/L (25 °C) (-) Klimisch score: 2
Log K <sub>ow</sub>	1.98 (ambient temperature) (Leo et al. 1971.Chem. Rev. 71:537-8.) Klimisch score: 2

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## Toxicological data

Sensitisation	<p>Positive for skin sensitization (24h after challenge (50%): grade 1 (5/20)) (48h after challenge (50%): grade 1 (5/20)) (48h after rechallenge (5%): grade 1 (2/20)) (Guinea pigs, Induction (epicutaneous) and Challenge (occlusive) - No guideline indicated but performed according to the Buehler guinea pig method) Klimisch score 1 (key study)</p> <p>No irritation or sensitisation in a dermal repeated insult patch test employing a panel of 50 human test persons (no guideline – old study (1976)) Klimisch score 2(key study)</p>
Repeated toxicity	<p><b>Oral</b> NOAEL 1500 mg/kg bw (male/females mice) LOAEL of 94 mg/kg bw/day (male/females rats) (renal toxicity - histopathological lesions) (No changes in sperm morphology and vaginal cytology evaluations – rats/mice) (0, 94, 187, 375, 750, 1500 mg/kg bw, oral (gavage), rat, mice, 90 day - EPA OPPTS 870.3100) Klimisch score 2 (key study) Read-across from tetrachlorophthalic anhydride</p> <p><b>Inhalation</b> NOAEC 2 mg/L air (male/female) LOAEC 8 mg/L air (male/female) (Salivation, lacrimation, nasal discharge, and nasal porphyrin discharge; decrease in liver weight; increase in lung weight was observed in both exposure levels; increase in relative adrenal and thyroid weight in females at 8 mg/L may have been compound-related. Microscopically, an increase in inflammatory lung lesions in both experimental groups may have been compound related) (Whole body inhalation exposures (0, 2, 8 mg/L) for 5d/wk for 3 weeks, rat – no guideline) Klimisch score 2 (key study)</p> <p><b>Dermal</b> NOAEL 500 mg/kg bw/d LOAEL 5000 mg/kg bw/d (All rabbits at high dose level died/sacrificed in extremis) (0, 50, 500 or 5000 mg/kg/d, 5 days/week for 4 weeks, rabbit – no guideline) Klimisch score 2 (key study)</p>
Mutagenicity/genotoxicity	<p>Negative in vitro in Bacterial Reverse Mutation Assay (+/- metabolic activation) (No guideline - Reported by the U.S. National Toxicology Program, performed according to good laboratory practices. Tests performed by two independent laboratories, each in triplicate) Klimisch score 1 (key study) Read-across from tetrachlorophthalic anhydride</p>



Negative in vitro in chromosome aberrations and sister chromatid exchanges assay using Chinese Hamster ovary cells (+/- metabolic activation) (No guideline - Reported by the U.S. National Toxicology Program, tested under good laboratory practices and published in the peer reviewed literature)  
Klimisch score 1 (key study) Read-across from tetrachlorophthalic anhydride

Ambiguous in vivo in chromosome aberrations and sister chromatid exchanges assay using mice (The number of SCE in treated animals were clearly below that in the positive control but increased slightly with each increasing dose) (i.p. - 0, 100, 200, 400 mg/kg)  
(No guideline - Reported by the U.S. National Toxicology Program and published in the peer reviewed literature).  
Klimisch score 1 (key study)  
Read-across from tetrachlorophthalic anhydride

No chromosome aberration in vivo using mice (sister chromatid exchanges in bone marrow - i.p. - 0, 100, 200, 400 mg/kg)  
(No guideline - Reported by the U.S. National Toxicology Program and published in the peer reviewed literature)  
Klimisch score 1 (key study)  
Read-across from tetrachlorophthalic anhydride

No gene mutation in vivo (sex-linked recessive lethal mutations in the fruit fly)  
(No guideline - Reported by the U.S. National Toxicology Program and published in the peer reviewed literature).  
Klimisch score 1 (key study)  
Read-across from tetrachlorophthalic anhydride

Endocrine

No data

Carcinogenicity

No data

Reproductive and developmental toxicity

Reproductive toxicity: No data

Developmental toxicity (EPA OPPTS 870.3700):  
NOEL (maternal toxicity) 3000 mg/kg bw/d  
NOEL (foetotoxicity toxicity) 3000 mg/kg bw/d  
LOAEL 10000 mg/kg bw/d (4/5 died by GD14; the fifth was gravid at sacrifice, bodyweight reduced)  
(30, 100, 300, 1000, 3000, 10000 mg/kg bw/d, oral (gavage), rat)  
Klimisch score 2 (key study)

Developmental toxicity (EPA OPPTS 870.3700):  
NOEL (maternal toxicity) 1000 mg/kg bw/d  
NOEL (foetotoxicity toxicity) 1000 mg/kg bw/d  
LOAEL 2000 mg/kg bw/d (body weight decrease, increase in ossification variations and vertebral or rib defects)  
(Tetrachlorophthalic anhydride: at doses of <= 1000 mg/kg bw administered daily on GD 6 - GD 19 to rats by gavage in corn oil induced no maternal toxicity,

	embryotoxicity, foetotoxicity or teratogenic effects) (0, 250, 1000, 2000 mg/kg/d, oral (gavage), rat) Klimisch score 2 (key study) Read-across from tetrachlorophthalic anhydride
Toxicokinetics/Metabolism	Toxicokinetics (rat – no guideline): A single oral dose of radioactive test article was administered to male and female rats. The test article was hydrolyzed to the acid form and partly absorbed in the gastro-intestinal tract. The absorbed portion was readily eliminated in the urine (~20%) within 24 hrs. and the unabsorbed portion was eliminated in the feces within 48 hrs. (~75%). The test article was rapidly distributed in the body and the rate of elimination in urine was proportional to the concentration in the blood. The rate constant for elimination was 0.081 and the half-life in blood was 8.5 hr. Overall, a low bioaccumulation potential. Klimisch score 2 (key study)
Other	No data
DNEL (W) oral	No data
DNEL (W) inhalation	0.64 mg/m <sup>3</sup> (long-term)
DNEL (W) dermal	7 mg/kg bw/day (long-term)
DNEL (G) oral	No data
DNEL (G) inhalation	No data
DNEL (G) dermal	No data
Classification proposed by the registrant	Skin Sens. 1 H317: May cause an allergic skin reaction.

## Ecotoxicological data

Algae	EC50 ( <i>Green algae</i> , 96 hours): 22.26 mg/L (hydrolysis product of TBPA (TBP acid)) (ECOSAR (v1.00) module of EPI v4.00-4.10) Klimisch score: 2
Crustaceans	EC50 ( <i>Daphnia magna</i> , 48 hours): > 5.6 mg/L (EPA OPPTS 850.1010 (Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids)) Klimisch score: 2  NOEC ( <i>Daphnia magna</i> , 16 days): = 2.631 mg/L (hydrolysis product of TBPA (TBP acid)) (ECOSAR module of EPIwin.) Klimisch score: 2

Fish	LC50 ( <i>Oncorhynchus mykiss</i> , 96 hours): > 10 mg/L (EPA OPP 72-1 (Fish Acute Toxicity Test)) Klimisch score: 2
	(Freshwater fish, 30d) = 2.235 mg/L (hydrolysis product of TBPA (TBP acid)) ECOSAR v1.00 module of EPIwin Klimisch score: 2
Terrestrial plants	-
Soil macroorganisms	-
PNEC (fresh water)	0.0056 mg/L (Assessment factor: 1,000)
PNEC (marine water)	0.00056 mg/L (Assessment factor: 10,000)
PNEC (fresh water sediment)	0.0831 mg/kg sediment dw (partition coefficient)
PNEC (marine water sediment)	0.00831 mg/kg sediment dw (partition coefficient)
PNEC (soil)	1.7 mg/kg soil dw (Assessment factor: 100)

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## Environmental fate

Bioconcentration factor (BCF)	0 (flow through, <i>Lepomis macrochirus</i> ) (Designed to conform to the then-most-recent draft of the Guidelines for Registering pesticides in the United States (Jan 30, 1978). Krezeminski et al. (1975. J. Agr. Food Chem 23:1060) and Schultz (1973. J. Agr. Food Chem 21:186) were used as guides.) Klimisch score: 2
Ready biodegradability	Not readily biodegradable (BIOWIN v.10, a module in EPI v3.20) Klimisch score: 1
Adsorption/desorption	Koc = 82.69 (Calculated: PCKOC v1.66 module of EPIwin) Klimisch score: 2

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## PBT

REACH registration dossier	The substance is not PBT / vPvB
QSAR	-

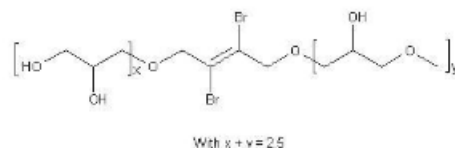
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# 2-butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydro-chlorinated, methoxylated

## Identification of substance

CAS No.	68441-62-3
EINECS No.	-
IUPAC name	2-Butyne-1,4-diol, polymer with 2-(chloromethyl)oxirane, brominated, dehydrochlorinated, methoxylated

Structure



SMILES

## REACH

Registration	Full
Submission	Individual Submission
Total tonnage	1,000 - 10,000 tonnes per annum
Harmonised classification	Not classified
Notified classification	In total 165 Notified classifications
	Acute Tox. 4 (H302)
	Eye Irrit. 2 (H319)
REACH registration classification	Not classified

## Physical-chemical characteristics

Molecular weight	- g/mole
Vapour pressure	0.0655 Pa at (20°C) (EU Method A.4 (Vapour Pressure); OECD Guideline 104 (Vapour Pressure Curve)) Klimisch score: 1
Henry's law constant	-
Water solubility	4.4 g/L (20°C, pH 3.6) (OECD Guideline 105 (Water Solubility); Klimisch score: 1
Log $K_{ow}$	-0.03-3.3 (25°C, pH7) (EU Method A.8 (Partition Coefficient) OECD Guideline 117 (Partition Coefficient (n-octanol / water), HPLC Method) Klimisch score: 1

## Toxicological data

Sensitisation	Not sensitizing (guinea pig maximisation test, Induction (intradermal), Challenge (epicutaneous, occlusive) - OECD 406) Klimisch score 1 (key study)
Repeated toxicity	<b>Oral</b> LOAEL of 417 mg/kg bw/day (male/females) (Increased liver weights (females and males at all dose levels) and enlarged thyroid glands in males (males at all dose levels, females at mid and high dose) (0, 417, 625, 938 mg/kg bw/day for 14 day dose range finding, oral (gavage), rat - OECD Guideline 425 “Acute Oral Toxicity: Up and Down Procedure”) Klimisch score 1 (key study)  <b>Inhalation</b> NOAEC 300 mg/m <sup>3</sup> (male/female) (90 day, inhalation (aerosol, nose only), rat, 0, 30, 100 and 300 mg/m <sup>3</sup> – OECD 413) (Klimisch score 1 (key study)  NOAEC (systemic effects) 300 mg/m <sup>3</sup> (male/female) LOAEC (systemic effects) 1000 mg/m <sup>3</sup> (male/female) (Haematology, clinical chemistry, organ weights, no histopathological changes) LOAEC (acute effects) 300 mg/m <sup>3</sup> (male/female) (Slight inflammation of the epithelial tissues of the upper respiratory tract and adaptation of these tissues (metaplasia) (28/14 day, inhalation (aerosol, nose only, 6 hours/day, 5 days/week ), rat, 0, 300, 1000 and 3000 mg/m <sup>3</sup> – OECD 412) (Supplementary sperm analysis showed no statistically significant changes in epididymal and testes sperm counts, effects were observed on epididymal sperm morphology) (Klimisch score 1 (key study)
Mutagenicity/genotoxicity	Positive (genotoxicity) in the in vitro Bacterial Reverse Mutation Assay (+ metabolic activation) (A dose related increase in the mean number of revertants were observed) (OECD Guideline 471) Klimisch score 1 (key study)  Positive (genotoxicity) in the in vitro mammalian cell gene mutation assay (+ metabolic activation) (Mutagenic at the TK-locus of mouse lymphoma L5178Y cells) (OECD Guideline 476) Klimisch score 1 (key study)  Negative (no DNA damage and/or repair) in the in vivo Unscheduled DNA Synthesis (UDS) Test with Mammalian Rat Liver Cells in vivo) (Inhalation 1.03 and 3.14 g/m <sup>3</sup> - OECD Guideline 486) Klimisch score 1 (key study)

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Negative (no clastogenic activity) in the in vivo micronucleus assay (750, 1500 and 3000 mg/kg bw, mice (male/female)- OECD Guideline 472)  
Klimisch score 1 (key study)

Endocrine	No data
Carcinogenicity	No data
Reproductive and developmental toxicity	<p>Reproductive toxicity: No data A Two-Generation Reproduction Toxicity Study (OECD Guideline 416) is proposed by the registrant based on tonnage band data requirements and awaits feedback from ECHA (deadline for comments 3/11-2014).</p> <p>Developmental toxicity: NOEL (maternal toxicity) 940 mg/kg bw/day (highest dose tested) NOEL (developmental toxicity) 940 mg/kg bw/day (highest dose tested) (0, 230, 470, 940 mg/kg bw/day, oral (gavage), rat – OECD 414) Klimisch score 1 (key study)</p> <p>A Prenatal developmental Toxicity Study in rabbits (OECD Guideline 414) is proposed by the registrant based on tonnage band data requirements and awaits feedback from ECHA (deadline for comments 3/11-2014).</p>
Toxicokinetics/Metabolism	No data
Other	No data
DNEL (W) oral	No data
DNEL (W) inhalation	6 mg/m <sup>3</sup> (long-term)
DNEL (W) dermal	0.87 mg/kg bw/day (long term)
DNEL (G) oral	0.435 mg/kg bw/day (long term)
DNEL (G) inhalation	1.5 mg/kg bw/day (long term)
DNEL (G) dermal	No data
Proposed classification by registrant	Eye Irrit. 2 H319: Causes serious eye irritation. Acute Tox. 4 H302: Harmful if swallowed

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## Ecotoxicological data

Algae	EC50 ( <i>Pseudokirchnerella subcapitata</i> , 96 hours): > 1000 mg/L (growth rate)
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NOEC (*Pseudokirchnerella subcapitata*, 96 hours): 250 mg/L (growth rate)  
(OECD Guideline 201 (Alga, Growth Inhibition Test))  
Klimisch score: 1

Crustaceans EC50 (*Daphnia magna* 48 hours): 520 mg/L  
(OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test))  
Klimisch score: 1

-

Fish LC50 (*Poecilia reticulata*, 96 hour): 560 mg/L  
(OECD Guideline 203 (Fish, Acute Toxicity Test))  
Klimisch score: 1

-

Terrestrial plants

-

Soil macroorganisms

-

PNEC (fresh water) 0.52 mg/L (Assessment factor: 1,000)

PNEC (marine water) 0.052 mg/L (Assessment factor: 10,000)

PNEC (fresh water sediment) 2.6 mg/kg sediment dw (partition coefficient)

PNEC (marine water sediment) 0.26 mg/kg sediment dw (partition coefficient)

PNEC (soil) 0.215 mg/kg soil dw (partition coefficient)

## Environmental fate

Bioconcentration factor (BCF)

-

Ready biodegradability

Not readily biodegradable (16%, 28d)  
OECD Guideline 301 D (Ready Biodegradability: Closed Bottle Test)  
Klimisch score: 1

Adsorption/desorption

-

## PBT

REACH registration dossier The substance is not PBT / vPvB

QSAR

-







### **Pre-screening of REACH registration dossiers for 9 brominated flame retardants**

This is a pre-screening of the toxicological and eco-toxicological effects, as presented in the REACH-registration dossiers, of 9 selected brominated flame retardants (BFRs) that were identified by the Danish Environmental protection Agency. It is a follow-up of the Danish EPA's List of Undesired Substances (LOUS) review 2012-2015. The background for implementing this project was the results from a survey of brominated flame retardants under LOUS (Environmental Project no. 1536 in 2014). Based on data available three BFR's were identified in the review as having a concern and as possible candidates for substance evaluation under REACH: BEH-TEBP (CAS: 26040-51-7), DBNPG (CAS: 3296-90-0) and HEEHP-TEBP (CAS: 20566-35-2). Concern was also identified for TBP (CAS: 118-79-6) and TTBP-TAZ (CAS: 25713-60-4), but other member states already are going to or have implemented risk reduction initiatives for these.

Dette er en foreløbig gennemgang af de toksikologiske og økotoxikologiske effekter angivet i REACH registrerings-dossiererne for 9 bromerede flammehæmmere (BFR'er), som er blevet identificeret af Miljøstyrelsen. Det er et opfølgingsprojekt i forbindelse med Miljøstyrelsens arbejde med Listen over uønskede stoffer (LOUS) 2012-2015. Baggrunden er at implementere dette projekt er resultaterne fra en kortlægning af BFR'er under LOUS (Miljøprojekt nr. 1536 i 2014). Der blev identificeret 3 BFR'er i gennemgangen, hvor der på baggrund af tilgængelige data er grund til bekymring og som derfor kan blive kandidater til stofvurdering under REACH: BEH-TEBP (CAS: 26040-51-7), DBNPG (CAS: 3296-90-0) and HEEHP-TEBP (CAS: 20566-35-2). Der blev også identificeret bekymring for TBP (CAS: 118-79-6) og TTBP-TAZ (CAS: 25713-60-4), men andre medlemslande skal eller har allerede igangsat risikoreduceringsinitiativer for disse.



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