SUBSTANCE EVALUATION CONCLUSION

as required by REACH Article 48

and

EVALUATION REPORT

for

Bis(2-ethylhexyl) tetrabromophthalate

EC No 247-426-5

CAS No 26040-51-7

Evaluating Member State: Sweden

Dated: 9 July 2020

Evaluating Member State Competent Authority

Swedish Chemicals Agency
Street address:
Esplanaden 3A
SE-172 67 Sundbyberg
Postal address:
Box 2
SE-172 13 Sundbyberg
Tel: +468-519 41 100
Fax: +468-735 76 98
Email: kemi@kemi.se
Website: http://www.kemi.se/en

Year of evaluation in CoRAP: 2019

Member State concluded the evaluation without any further need to ask more information from the registrants under Article 46(1) decision.

Further information on registered substances here:

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

DISCLAIMER

This document has been prepared by the evaluating Member State as a part of the substance evaluation process under the REACH Regulation (EC) No 1907/2006. The information and views set out in this document are those of the author and do not necessarily reflect the position or opinion of the European Chemicals Agency or other Member States. The Agency does not guarantee the accuracy of the information included in the document. Neither the Agency nor the evaluating Member State nor any person acting on either of their behalves may be held liable for the use which may be made of the information contained therein. Statements made or information contained in the document are without prejudice to any further regulatory work that the Agency or Member States may initiate at a later stage.

Foreword

Substance evaluation is an evaluation process under REACH Regulation (EC) No. 1907/2006. Under this process the Member States perform the evaluation and ECHA secretariat coordinates the work. The Community rolling action plan (CoRAP) of substances subject to evaluation, is updated and published annually on the ECHA web site[1].

Substance evaluation is a concern driven process, which aims to clarify whether a substance constitutes a risk to human health or the environment. Member States evaluate assigned substances in the CoRAP with the objective to clarify the potential concern and, if necessary, to request further information from the registrant(s) concerning the substance. If the evaluating Member State concludes that no further information needs to be requested, the substance evaluation is completed. If additional information is required, this is sought by the evaluating Member State. The evaluating Member State then draws conclusions on how to use the existing and obtained information for the safe use of the substance.

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the final outcome of the Substance Evaluation carried out by the evaluating Member State. The document consists of two parts i.e. A) the conclusion and B) the evaluation report. In the conclusion part A, the evaluating Member State considers how the information on the substance can be used for the purposes of regulatory risk management such as identification of substances of very high concern (SVHC), restriction and/or classification and labelling. In the evaluation report part B, the document provides explanation how the evaluating Member State assessed and drew the conclusions from the information available.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating Member State. In case the evaluating Member State proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating Member State, it does not preclude other Member States or the European Commission from initiating regulatory risk management measures which they deem appropriate.

[1] http://echa.europa.eu/regulations/reach/evaluation/substance-evaluation/community-rolling-action-plan

Contents

Part A. Conclusion

1. CONCERN(S) SUBJECT TO EVALUATION

Bis(2-ethylhexyl) tetrabromophthalate (TBPH) was originally selected for substance evaluation in order to clarify concerns about:
-Potential endocrine disruptor
-Suspected PBT/vPvB
-Wide dispersive use
-Exposure of environment

No additional concerns were identified during the evaluation.

2. OVERVIEW OF OTHER PROCESSES / EU LEGISLATION

A testing proposal evaluation was performed in 2015 and resulted in a request for a pre-natal developmental toxicity study (test method: OECD 414) in rats or rabbits via the oral route.
A compliance check (CCH) was performed and a decision was sent to the Registrant(s) in 2016 with requests for a sub-chronic toxicity study (90-day), an *in vitro* gene mutation study in bacteria, a screening study for reproductive/developmental toxicity (OECD 421 or 422) and a dietary bioaccumulation study. In response to the requests in the CCH decision the Registrant(s) provided the requested information including a waiver for the screening study for reproductive/developmental toxicity which was accepted by ECHA.
Also, the registration was updated with assessments of the potential endocrine disrupting properties of TBPH for the environment and human health.

3. CONCLUSION OF SUBSTANCE EVALUATION

The evaluation of the available information on the substance has led the evaluating Member State to the following conclusions, as summarised in the table below.

Table 1

CONCLUSION OF SUBSTANCE EVALUATION	
Conclusions	**Tick box**
Need for follow-up regulatory action at EU level	x
Harmonised Classification and Labelling	
Identification as SVHC (authorisation)	x
Restrictions	
Other EU-wide measures	
No need for regulatory follow-up action at EU level	

4. FOLLOW-UP AT EU LEVEL

4.1. Need for follow-up regulatory action at EU level

4.1.1. Harmonised Classification and Labelling

Not applicable

4.1.2. Identification as a substance of very high concern, SVHC (first step towards authorisation)

The evaluating Member State (eMSCA) considers that TBPH meets the REACH Annex XIII vPvB criteria based on a weight of evidence approach including all available information (i.e. QSAR-predictions, laboratory studies, monitoring data). The use profile of TBPH suggests a potential for widespread dispersive release to the environment. TBPH has been detected in biota worldwide including Europe. It has also been detected in plasma and milk from nursing women in Canada. Furthermore, the findings in arctic species such as ringed seal and polar bear indicates the TBPH has a long-range transport potential.

TBPH is considered to be of relevance under the SVHC Roadmap to 2020 (Table 2).

Table 2: SVHC Roadmap 2020 criteria

	Yes	*NO*
a) Art 57 criteria fulfilled?	*X*	
b) Registrations in accordance with Article 10?	*X*	
c) Registrations include uses within scope of authorisation?	*X*	
d) Known uses not already regulated by specific EU legislation that provides a pressure for substitution?		*X*

The SE CA therefore considers it appropriate to prepare and submit an SVHC dossier. This would enable formal identification of TBPH as an SVHC.
The registrants do not consider that TBPH meets the Annex XIII criteria, so SVHC identification would create legal certainty and oblige the registrants to review their risk management measures and provide advice on safe use to downstream users.
Furthermore article importers would be obliged to notify ECHA of TBPH imports (in articles) exceeding 1 tonne per year, where the concentration in the article exceeds 0.1% (w/w).

4.1.3. Restriction

4.1.4. Other EU-wide regulatory risk management measures

Not applicable

5. CURRENTLY NO FOLLOW-UP FORESEEN AT EU LEVEL

5.1. No need for regulatory follow-up at EU level

Not applicable, see section 4.

5.2. Other actions

Not applicable, see section 4.

6. TENTATIVE PLAN FOR FOLLOW-UP ACTIONS (IF NECESSARY)

Indication of a tentative plan is not a formal commitment by the evaluating Member State. A commitment to prepare a REACH Annex XV dossier (SVHC, restrictions) and/or CLP Annex VI dossier should be made via the Registry of Intentions.

Table 3

FOLLOW-UP		
Follow-up action	**Date for intention**	**Actor**
RMOA	TBD	Sweden
SVHC dossier	TBD	Sweden

Part B. Substance evaluation

7. EVALUATION REPORT

7.1. Overview of the substance evaluation performed

Bis(2-ethylhexyl) tetrabromophthalate (TBPH) was originally selected for substance evaluation in order to clarify concerns about:

-Potential endocrine disruptor

-Suspected PBT/vPvB

-Wide dispersive use

-Exposure of environment

Table 4

EVALUATED ENDPOINTS	
Endpoint evaluated	**Outcome/conclusion**
PBT/vPvB	vPvB properties confirmed.
Endocrine disruption for human health	Not further investigated and unresolved No further action.
Endocrine disruption for the environment	Not confirmed. No further action.

7.2. Procedure

TBPH was included in the Community Rolling Action Plan (CoRAP) for evaluation in 2019. The initial concerns were suspected PBT/vPvB, potential endocrine disruptor, wide dispersive use, and exposure of the environment. The evaluation started in April 2019 using the Lead registrant's dossier from March 2019. An extensive literature search was performed in the autumn 2019 mainly focused on finding monitoring data.

A draft conclusion on the persistence and bioaccumulation properties was circulated to the PBT EG for comments in a written procedure in December 2019. Another written consultation with the PBT EG was performed in May 2020.

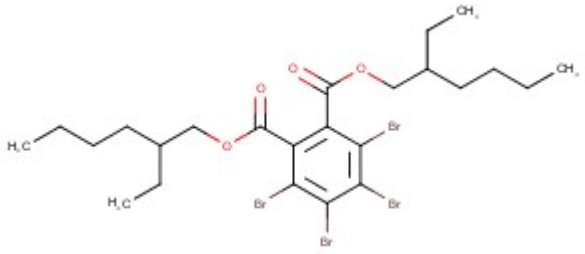
7.3. Identity of the substance

Table 5

SUBSTANCE IDENTITY	
Public name:	Bis(2-ethylhexyl) tetrabromophthalate
EC number:	247-426-5
CAS number:	26040-51-7
Index number in Annex VI of the CLP Regulation:	_
Molecular formula:	C24H34Br4O4
Molecular weight range:	706 g/mol
Synonyms:	TBPH BEHTBP

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

Structural formula:



7.3.1. Similar substances, grouping and read across

7.3.1.1. Brominated phthalates

TBPH is one of several brominated phthalates that are used as flame retardants. The U.S. EPA assessed a group of seven brominated phthalates for problem formulation and data needs assessment (US EPA, 2015). In addition to TBPH, TBB (CAS RN 183658-27-7), TBPA-diol (CAS RN 20566-35-2), TBPA Diol-mixed esters (CAS RN 77098-07-8) and Bis(2,3-dibromopropyl) phthalate (CAS RN 7415-86-3) were included in the group.
The major use identified for all these substances was as flame retardant in polyurethane foams (PUFs) and PUF products. The assessment states that these chemicals have similar physical and chemical properties and environmental fate characteristics. The group members are expected to be persistent, bioaccumulative and potentially hazardous to human health, and to the environment. It was concluded that the available data on the toxicological hazard of these chemicals is incomplete for risk assessment.

Additionally, a report is available from the Danish EPA which has applied a category approach to 67 brominated flame retardants, including TBPH (Wedebye *et al*., 2016). The chemicals were divided into 15 groups, based on structural similarity. TBPH was assigned to the group of "Phthalates/benzoates" together with TBB (CAS RN 183658-27-7), TBPA-diol (CAS RN 20566-35-2) and Bis(methyl)tetrabromophthalate (CAS RN 55481-60-2). All members were predicted to be persistent and to have positive indications for carcinogenicity and weak genotoxicity.

7.3.1.2. Read-across to bis(2-ethylhexyl) phthalate (DEHP)

TBPH is the brominated analogue of DEHP. DEHP has been widely used as a plasticizer but is currently a restricted substance due to its endocrine disrupting properties and reproductive toxicity. Structural similarity to DEHP raised a concern for toxicity of TBPH. However, bromination alters the physical and chemical properties of DEHP. Available data e.g. a 28 d repeated dose toxicity study in which both TBPH and DEHP were tested indicate that the toxicity pattern of DEHP is different from that of TBPH..

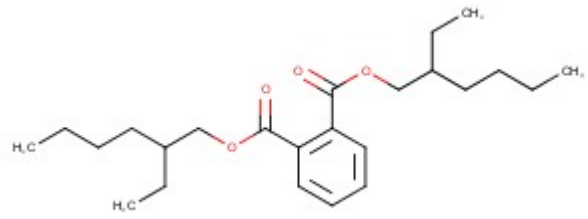
In photodegradation experiments TBPH has been shown to undergo sequential reductive debromination, possibly down to non-brominated degradation products (Davis and Stapleton, 2009, see section 7.7.1). However, there is limited evidence of debromination of TBPH *in vivo*.

Table 6

READ-ACROSS SUBSTANCE IDENTITY	
Public name:	Bis(2-ethylhexyl) phthalate (DEHP)
EC number:	204-211-0
CAS number:	117-81-7
Index number in Annex VI of the CLP Regulation:	607-317-00-9
Molecular formula:	C24H38O4
Molecular weight range:	390 g/mol
Synonyms:	DEHP 1,2-bis(2-ethylhexyl) benzene-1,2-dicarboxylate 1,2-Benzenedicarboxylic acid bis (2-ethylhexyl) ester

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

Structural formula:



7.4. Physico-chemical properties

Table 7

OVERVIEW OF PHYSICOCHEMICAL PROPERTIES (TBPH)	
Property	**Value**

Physical state at 20°C and 101.3 kPa	Colourless slightly viscous liquid
Vapour pressure	$3.56E^{-7}$ Pa at 25°C MPBPWIN
Water solubility	6.2×10^{-2} ng/l (WSKOW v1.42, Log Kow 10.2) 1.9 ng/l (WSKOW from fragments) <0.05 µg/l OECD TG 105 (flask method) 794 µg/l (1% acetonitrile as solubilizer) OECD TG 105 (flask method)
Partition coefficient n-octanol/water (Log Kow)	10.2 OECD TG 117
Log Koc	5.9 (KOCWIN MCI method) 6.4 (KOCWIN, Kow method using measured Log Kow) 7.3 OECD TG 121 (HPLC metod)
Log Koa	15.114 (KOAWIN v11.10 using measured Log Kow)
Flammability	Not relevant
Explosive properties	Not relevant
Oxidising properties	Not relevant
Granulometry	Not relevant
Stability in organic solvents and identity of relevant degradation products	No information
Dissociation constant	Not relevant

7.5. Manufacture and uses

7.5.1. Quantities

Table 8

AGGREGATED TONNAGE (PER YEAR)				
☐ 1 – 10 t	☐ 10 – 100 t	☒ 100 – 1000 t	☐ 1000- 10,000 t	☐ 10,000-50,000 t
☐ 50,000 – 100,000 t	☐ 100,000 – 500,000 t	☐ 500,000 – 1000,000 t	☐ > 1000,000 t	☐ Confidential

7.5.2. Overview of uses

According to the registration information on the ECHA dissemination webpage TBPH is used in articles and mixtures by professional workers (widespread uses).

Use information is also available from other sources including the US EPA.
TBPH is used as additive flame retardant. It is one of the two brominated chemicals in Firemaster 550 (TBPH:TBB ratio approx. 20-30:70-80), the primary replacement for pentabromodiphenyl ether (pentaBDE) in polyurethane foam (PUF).
The substance is also used as a flame retardant and as a plasticizer for flexible polyvinylchloride and for use in wire and cable insulation, film and sheeting, carpet backing, coated fabrics, wall coverings and adhesives.

Table 9: Information from the ECHA dissemination webpage 2020-04-15

USES	Use(s)
Formulation	Formulation of adhesives, sealants Formulation of preparations Formulation in materials
Uses at industrial sites	Used in production of rubber articles Use of plastics, masterbatch or compound in calendaring applications Application of adhesives
Uses by professional workers	Application of reactive sealants and adhesives One component foam (spray/dose can) Laboratory use
Consumer Uses	-
Article service life	Plastic or rubber articles Electrical/electronic articles Machinery, mechanical appliances One component foam

7.6. Classification and Labelling

7.6.1. Harmonised Classification (Annex VI of CLP)

None.

7.6.2. Self-classification

- In the registration(s): Not classified
- The following hazard classes are in addition notified among the aggregated self-classifications in the C&L Inventory: Eye Irrit. 2

7.7. Environmental fate properties

7.7.1. Degradation

Hydrolysis

The hydrolytic stability of TBPH has been studied in a study performed according to OECD guideline 111. The water solubility of TBPH is < 0.05 µg/l and therefore an aqueous solution with 1% acetonitrile of 0.4 mg TBPH/l was used (TBPH solubility in 1% acetonitrile solution is 794 µg TBPH/L). Only the preliminary phase of the study where the hydrolysis at pH 4, 7 and 9 at 50°C is determined was performed. The disappearance of the test item was > 91% after the study period at each pH. The resulting half-lives were 30.4 h at pH 4, 44.1 h at pH 7 and 77.5 at pH 9. The registrant used the van´t Hoff equation to extrapolate the half-lives to a temperature of 20°C which gave the following values: 10.1 days at pH4, 14.7 days at pH7 and 25.8 days at pH9. One transformation product, tetrabromophthalic acid, was identified but not quantified. The identification of the metabolite was performed in a second experiment performed at 60°C and pH 4. The registrant has given this study reliability 1. The evaluating Member State disagrees and considers this study unreliable as it is only a preliminary study that should have been followed up by a definitive study performed at least three different temperatures according to the guideline.

In contrast to the hydrolysis study referred to in the previous paragraph, Environment and Climate Change Canada, Health Canada (2019) in their evaluation of TBPH refers to an unpublished industry hydrolysis study (not available to the evaluating Member State) where half-lives > 1 year at pH 4,7 and 9 at a temperature of 50°C are reported.

Photolysis

No information on photolysis in air, soil or water is included in the registration dossier. AopWin v1.92 estimates the half-life for atmospheric oxidation to 5.8 hours. However, the model predicts that ≥99.8% will be sorbed to airborne particulates and that the sorbed fraction may be resistant to atmospheric oxidation. Because the sorbed fraction is likely to be resistant to atmospheric oxidation, the AOPWIN half-life value based on reaction with hydroxyl radicals is most probably an underestimation of the half-life in air. The sorbed fraction to particulates may increase its residence time and potential for long-range transport

Davis and Stapleton (2009) studied the photodegradation of nonabrominated diphenyl ethers, 2- ethyl hexyltetrabromobenzoate (TBB) and TBPH. The substances dissolved in either toluene, methanol or tetrahydrofuran were added to glass vials which were exposed to sunlight in the summer and early fall of 2008. The study took place in Durham, North Carolina and the average solar radiation during the test period was 687.5 W/m^2. Three vials were sampled after 5, 15, 30, 60 and 240 min of sunlight exposure. The half-life for TBPH was 147 min in toluene, 220 min in Methanol and 168 min in Tetrahydrofuran. The authors report that three tribrominated and two dibrominated isomers appeared to have been formed through the degradation of TBPH.

The available information indicates that TBPH can be photolytically degraded. However, considering the very low vapour pressure, photolysis in the atmosphere is not considered to be a relevant degradation pathway. However, TBPH has frequently been detected in air also in remote areas. In most cases detectable only in the particulate phase of the air samples. The sorbed fraction is likely to be resistant to atmospheric oxidation.

Biodegradation

Estimated data

No estimated data were included in the registration dossier. However, Biowin gives the following predictions for TBPH:
Biowin 2: 0.1319
Biowin 3: 1.9718
Biowin 6: 0.0945

According to REACH guidance R.11 these Biowin predictions indicate that TBPH is potentially persistent or very persistent.

Screening tests

The registration dossier contains no ready biodegradation studies. However, USEPA lists results from two ready biodegradation studies in an assessment of alternatives to pentabromodiphenyl ether (PBDE) (USEPA, 2015). One study according to OECD TG 301D gave less than <4% ThOD after 10 days. The other study, a closed bottle test (OECD 301B) gave 2% degradation as measured by CO2 production after 28 days. The evaluating Member State has not had access to these studies. No details on the studies are given in the report but USEPA considers them to be "adequate guideline studies"

The registration dossier includes one inherent biodegradability test according to OECD guideline 302 C (Modified MITI test).A mixture of activated sludge from two different wastewater treatment plants treating predominantly domestic wastewater and activated sludge from a wastewater treatment plant treating predominantly industrial wastewater

was used as inoculum. The three sludge types were mixed taking 2 parts from each of the two domestic WWTPS plus 1 part from the industrial WWTP. (Addition of 20% sludge from an industrial wastewater plant may have made the conditions for degradation more favourable than if only domestic sludge had been used.) Continuously stirred 250 ml closed flask (three replicates) were incubated for 28 days in the dark at 25 ± 2°C. The concentration of inoculum was 100 mg /L and the TBPH concentration was 30 mg/L. A control (inoculum only) and a positive control (sodium benzoate) were run in parallel. The biodegradation was estimated by measuring the O_2 consumption.

The degradation of TBPH was 6% after 7 days and 7% after 28 days. The degradation of the reference compound sodium benzoate reached 65 % after 7 days but remained 2 % below the level of ≥ 65 % after 14 days. This is according to the authors caused by high activity of the sludge in the blank control. Despite this the test is considered to be valid. TBPH is "Not Inherently Biodegradable".

Simulation tests

One study, De Jourdan *et al.* (2013), was located in the open literature although it is a mesocosm study and not a simulation study performed according to OECD guideline 308. The authors report a DT_{50}>200d for TBPH in sediment from this outdoor mesocosm study. The study was performed at The Guelph Turfgrass Institute in Ontario Canada that has a climate comparable to the northern parts of the European continent. The mean air temperature in this area of Canada is normally around 22°C in July, 21° C in August and 15°C in September. The mesocosms had a depth of 1.2 m, a diameter of 3.9 m and were filled with water to approximately 1 m (ca 12000 L). Artificial sediment containing organics-rich soil (1:1:1 mixture of topsoil:manure:compost organic content 10% dw) was placed on trays 52.1 x 25.4 x 5.7 cm and were placed on the bottom of each mesocosm so that > 50% of bottom surface was covered. This fate study took place over two years, with the mesocosms being established in May 2008, and treated in July 2008, and again in July 2009, with year 1 serving for method development purposes.
In year 1 Firemaster BZ-54 (TBPH:TBB 1:4) was applied to the water phase of three mesocosms by subsurface injection. The simultaneously application of TBPH and TBB is not expected to have affected the results of this study. Five injections were made at several locations in the mesocosms in an effort to achieve homogeneous distribution of the compound aiming at a nominal concentration of 0.03 mg/L which is at least an order of magnitude above the water solubility of < 0.05 µg/l (to achieve a target concentration of 500 ng TBPH/g sediment in the upper 5 cm on partitioning). Year 2 (July 16, 2009), two mesocosms from each treatment were retreated at the same concentration. Sediment samples and water samples (for analysis of particulate matter) were collected in triplicate during July to September 2009 (days 1, 4, 7, 14, 28, 42 and 70 after the treatment 16 July year 2). The mean recovery rate of the analysis method was 77.4 % with a standard deviation of 5.9%.
There were large fluctuations in TBPH concentration in the particulate matter throughout the study and the data did not fit first-order kinetics very well, with an r^2 value of 0.06. The concentration in the sediment did not fluctuate in the same manner with the maximum concentration being almost equal to the mean concentration during the whole sampling period. Regression equations (not shown in the publication) were used to estimate the median dissipation time (DT_{50}) of the compound. The DT_{50} in the particulate matter was estimated to 25 d. For the sediment, the regression equations were not significant, suggesting no significant decline. The authors of the study report the result as >200 d. The actual DT_{50} estimation gave a value of 9303 (1330 - 17280) days.
However, some degradation may have occurred in the particulate matter. There was one major unknown peak in the chromatogram which agreed fairly well with the expected mass of a tribrominated anhydride. This could have been formed via hydrolysis of the ester groups to tetrabromo phthalic acid subsequently forming an anhydride. The authors speculate that this could be due to photolysis in the particulate compartment as debrominated analogues of TBPH were detected in a photolysis study by Davis and Stapleton (2009), see paragraph on photolysis above.

The results from this study should be treated with care as a number of physical, experimental and analytical factors (e.g. sediment-to-water diffusion and resuspension, inhomogeneous distribution in the mesocosms, matrix interference) likely contributed to the level of uncertainty in determining the dissipation times. However, the study strongly indicates that TBPH is very persistent in sediment.

Degradation data for similar substances

The evaluating Member State have searched for degradation data on similar substances but there is very limited information available.

There are two other brominated phthalates registered in REACH. 2-(2-hydroxyethoxy)ethyl 2-hydroxypropyl 3,4,5,6-tetrabromophthalate (TBPA-Diol) (EC number 243-885-0) and TBPA Diol (mixed esters) (EC number 616-436-5). TBPA-Diol is registered at 1-10 tpa and there are no data in the dossier.

TBPA Diol (mixed esters) is an UVCB that contains constituents that are similar to TBPH. It is registered at 100 – 1000 tpa but the dossier contains virtually no test data. ECHA has performed a CCH with 15 data requests including a simulation test. The deadline for delivering the data is June 2022.

Tetrabromophthalic anhydride (EC number 211-185-4), theoretically a metabolite of TBPH, is also registered in REACH at 100-1000 tpa. For this substance the registration dossier contains an old soil study from 1979. The study reports hydrolysis of the anhydride to tetrabromophthalic acid but no biodegradation during 28 days.

For 2-Ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB) which is not registered in the EU there are some data available. TBB is used together with TBPH in flame retardant formulations such as Firemaster 500. Photolysis studies shows that TBPH is more stable than TBB (Davis and Stapleton, 2009). TBB was also included in the mesocosm study by de Jourdan *et al.* (2013). TBB had a shorter DT50 in the particulate matter than TBPH, 9 days compared to 25 d for TBPH. In sediment where TBPH had a DT50 > 200 days TBB was not detectable despite being applied at least at a 4 times higher dose.

Discussion/conclusion

A hydrolysis study sponsored by the registrant reports a DT_{50} of 14.7 days for TBPH in a 1% acetonitrile solution at pH7 and 20 °C extrapolated from 50°C with van´t Hoffs equation. Based on this study the registrant concludes that TBPH is rapidly hydrolysed in the environment and therefore not fulfils the P/vP criteria of REACH. This study was however only the preliminary part of an OECD guideline 111 study and therefore not considered fully reliable by the evaluating Member State. Furthermore, contradictory to this a hydrolysis half-life > 1year at pH 4,7 and 9 is reported by Canadian authorities in their evaluation of TBPH (Environment and Climate Change Canada, Health Canada 2019). Worth noticing is that DEHP (the unbrominated skeleton of TBPH) is reported to have a hydrolysis half-life > 2000 years according to the fact sheet on ECHAs dissemination web page. While read across may not be possible this indicates that the hydrolysis of TBPH may not be rapid.

TBPH has a very low water solubility <0.05µg/l and the hydrolysis study that gave measurable half-lives at 50 °C was performed with a 1% acetonitrile solution to enhance the water solubility. The relevance of this study can therefore be questioned. Furthermore, due to its low solubility and high Koc TBPH will be sorbed to particles and mainly distributed to sediment in the aquatic environment. Mackay Level III distribution modelling predicts that only approx. 2% will be distributed to water even if all emission are assumed to be to water (see Table 10). Therefore, hydrolysis is not considered to be a relevant degradation mechanism for TBPH.
The available information indicates that TBPH can be photolytically degraded. However, TBPH has a very low vapour pressure and is not expected to distribute to the gas phase of the atmosphere which is confirmed by the frequent findings of the substance in the particulate phase of the atmosphere, also in remote areas. The evaluating Member state

therefore concludes that photodegradation in the atmosphere is not a relevant removal process for TBPH.

Biowin predictions indicate that TBPH is persistent or very persistent to biodegradation. Two ready biodegradation tests referred to by the USEPA show that TBPH is not ready biodegradable (< 4% degradation). This is confirmed by the results from an enhanced ready test performed according to OECD guideline 302C at 25°C, which gave 7% degradation in 28 days despite that the conditions may have been more favourable than proposed in the guideline.

The REACH guidance R11 states "*Lack of degradation (<20% degradation) in an inherent The biodegradability test equivalent to the OECD TG 302 series may provide sufficient information to confirm that the P-criteria are fulfilled without the need for further simulation testing for the purpose of PBT/vPvB assessment. Additionally, in specific cases it may be possible to conclude that the vP-criteria are fulfilled with this result if there is additional specific information supporting.*"

In addition to the screening studies de Jourdan *et al* (2013) reports a sediment DT50> 200 days from an outdoor mesocosm study indicating that TBPH may be very persistent in sediment. This study is not a guideline study and the results have to be treated with care as inhomogeneous distribution in the mesocosms and several processes e.g. sediment-to-water diffusion and resuspension may have influenced the results. However, despite this the results indicates that TBPH is very slowly degraded in sediment.

There is very limited information available for other brominated phthalates or similar substances. Tetrabromophtalic anhydride, a theoretical degradation product of TBPH, appears to be persistent. The registration dossier for this substance contains results from a soil study from 1979. This study reports hydrolysis of the anhydride to tetrabromophtalic acid but no further biodegradation during 28 days.

TBPH has been detected in all compartments of the environment including air, surface water, sediment, and biota mostly in urban areas (see section **Error! Reference source not found.**). This is not in itself evidence of persistence. However, TBPH is present also in remote areas. It has been detected in the particulate phase of air in e.g. the East Greenland Sea, Svalbard, the Tibetan plateau and the Canadian arctic (Möller *et al* 2011a, Salamova *et al* 2014, Xiao *et al* 2012). TBPH has also been detected in water samples taken in the East Greenland Sea, although in very low concentrations (Möller *et al* 2011a). cf *et al* (2010) detected TBPH in several fish and bird species and in the liver of Ringed seal sampled in the Norwegian arctic. KLIF (2013) reports TBPH in 95% of the plasma samples from Polar bears in Svalbard and Vorkamp *et al.* (2015), detected TBPH in Black Guillemot eggs and Polar bear adipose tissue in samples taken in Central East Greenland 2012. The findings in biota are detailed in section 7.7.3. Besides showing that TBPH has a potential for long-range transport, the detection of TBPH in air, water and biota in remote areas without known local sources adds to the evidence that TBPH is very persistent.

Overall, based on the available information the evaluating Member state considers that TBPH fulfils the vP criterion of REACH.

7.7.2. Environmental distribution

When run with equal emissions to air, water and soil the Episuite Fugacity Level III model predicts that TBPH is mainly distributed to soil and sediment. This is the case also when the model is run with emissions only to air or water (see Table 10).

Table 10: Episuite Fugacity level III output (EQC default) for TBPH (using the values for physical/chemical properties calculated by Episuite)

	Mass amount (%)	**Emissions** (kg/h)
Equal emissions to air, water, and soil		
Air	0.0654	1000
Water	1.3	1000
Soil	34.2	1000
Sediment	64.4	0
Emissions to air only		
Air	0.7	1000
Water	0.4	0
Soil	78.5	0
Sediment	20.4	0
Emissions to water only		
Air	$1.1x10^{-10}$	0
Water	1.98	1000
Soil	$1.2x10^{-8}$	0
Sediment	98	0
Emissions to soil only		
Air	0	0
Water	0	0
Soil	100	1000
Sediment	0	

Abiotic monitoring

Air

Several publications report findings of TBPH in air despite its low vapour pressure. TBPH has been detected in air both in urban areas as well as in remote areas including the arctic. TBPH is predominantly found in the particulate phase of the air samples. The results from the studies cited below are compiled in Table 11.

In Oslo (Schlabach,2011) TBPH was detected in 5 of 12 samples with an average concentration of 23.9 pg/m^3 (std dev 36.9 pg/m^3).

Ma *et al* 2011, reported TBPH levels in air from six sites near the shores of the Great Lakes in USA. TBPH was not detected in the gas phase (detection limit 0.05 pg/m^3) but was detected in the particle phase in almost half of the samples collected from 2008 to 2010. In Urban areas, such as Chicago and Cleveland, the detection frequency was 93 and 99%, respectively with concentration ranging from 0.36 to 290 pg/m^3. In more remote areas the detection frequency ranged from 49 – 73% with concentrations ranging from 0.05 to 32 pg/m^3.

In a follow up study Liu *et al* 2016 air (vapour and particle phase) analysed samples from the same sites from 2008 to 2013 in order to investigate the time trends. The authors concluded that the concentrations of TBPH at all sites, except the more remote location, Sleeping Bear Dunes, increased with doubling times of 4–8 years during the sampling period.

Shoieb *et al* 2014, monitored TBPH for over one year at an urban site in Toronto, Canada during 2010 and 2011. TBPH was exclusively detected in the particle phase with a detection frequency of 87%. The median air concentration 0.26 pg/m^3.

Arinaitwe *et al* 2014 collected air and precipitation samples close to the shore of Lake Victoria at Entebbe, Uganda, between October 2008 and July 2010. The levels of TBPH showed an increasing trend. TBPH was not detected in 2008. In 2009 it was detected in

16% of the samples with an arithmetic mean of 3.39 pg/m^3. In 2010 the detection frequency was 88% with a mean of 18.2 pg/m^3.

Li *et al* 2016 detected TBPH in the particle phase of 75% of air samples taken in northeast China. The mean concentration was 30 ± 200 pg/m^3 (range: nd–2600 pg/m^3).; The detection frequency in the gas phase was 17% with a mean concentration of 1.1 ± 2.2 pg/m^3 (range: nd-2.2 pg/m^3).

Möller *et al* 2011a, investigated the spatial distribution of polybrominated diphenyl ethers (PBDEs) and several alternative non-PBDEs in air and seawater in the East Greenland Sea. TBPH was not detected in the gas phase but in the particulate phase with concentrations ranging from n.d to 0.02 pg/m^3. The detection frequency was 40%.

Möller *et al*, 2011b also analysed the occurrence of brominated flame retardant including TBPH in marine boundary layer air during a polar expedition from the East China Sea to the Arctic. TBPH was detected at a few stations only but with maximum concentrations of 8.9, 1.6, and 3.4 pg/m^3, respectively.

During a sampling cruise from the East Indian Archipelago toward the Indian Ocean and further to the Southern Ocean (November 2010 to March 2011) Möller *et al* (2012) investigated the occurrence, distribution, and temperature dependence in the marine atmosphere of several alternative brominated flame retardants (BFRs) including TBPH was detected in 90% of the samples (n=20) and only in the particulate phase. The concentrations ranged from not detected) to 2.8 pg/m^3. There was no clear distribution pattern.

Salamova *et al*, 2014 measured TBPH in the particle phase of atmospheric samples(N=34) collected at Longyearbyen on Svalbard from September 2012 to May 2013. The detection frequency was 88%, the mean concentration was 2.7 ± 0.49 pg/m^3 (range 0.27-14 pg/m^3).

Xiao *et al* 2012, monitored atmospheric concentrations of halogenated flame retardants for approximately one year at two remote stations, Nam Co on the Tibetan Plateau and Alert in the Canadian High Arctic. The average TBPH concentrations at Alert and Nam Co were 0.80 and 0.38 pg/m^3, respectively. The ranges at both sites were similar, in the magnitude of 0.1-1.5 pg/m^3.

Yu *et al* 2015, collected air samples at Little Fox Lake (LFL) in Canada's Yukon Territory from August 2011 to December 2014. TBPH was detectable in ~40% of the samples with an average concentration of 0.86 pg/m^3.

Table 11: TBPH levels in air

Site	**n**	**% detect**	**Range** (pg/m^3)	**Mean ± SD** (pg/m^3)	**Geomean** (pg/m^3)	**Ref**
Urban areas						
Oslo	12	42		23.9 ±36.9		Schlabach 2011
Chicago	86	93	0.36-76	6.2 ± 1.2	3.1	Ma *et al* 2011
Chicago		85			3.4 ± 0.5	Liu *et al* 2016
Cleveland	76	99	0.47-290	14 ± 5	3.8	Ma *et al* 2011

Cleveland		83			4.1 ± 0.6	Liu *et al* 2016
Toronto		87		0.26		Shoeib *et al* 2014
Rural areas						
Sturgeon Point	95	73	0.14-17	0.90 ± 0.24	0.52	Ma *et al* 2011
Sturgeon Point		75			0.58 ± 0.13	Liu *et al* 2016
Eagle Harbor	100	61	0.13-32	1.1 ± 0.5	0.42	Ma *et al* 2011
Eagle Harbor		69			0.53 ± 0.09	Liu *et al* 2016
Sleeping Bear Dunes	100	49	0.11-16	1.1 ± 0.4	0.45	Ma *et al* 2011
Sleeping Bear Dunes		63			0.46 ± 0.16	Liu *et al* 2016
Point Petre	45	53	0.18-3.7	0.79 ± 0.19	0.53	Ma *et al* 2011
Lake Victoria at Entebbe		0 (2008) 17 (2009) 88 (2010)	-	- 3.39 18.2	-	Arinaitwe *et al* 2014
Northeast China		75 (particle phase	nd–2600	30 ± 200		Li *et al* 2016
Northeast China		17 (gas phase)	nd-2.2	1.1 ± 2.2		Li *et al* 2016
Remote areas						
East Greenland sea		40 (particle phase) n.d (gas phase)	n.d.–0.08			Möller, 2011a
East China sea - arctic		Few detects	Max conc 1.6 3.4 8.9			Möller, 2011b
Indian ocean-Southern ocean	20	90 (particle phase)	n.d – 2.8			Möller, 2012
Svalbard	34		0.27-14	2.7 ± 0.49		Salamova *et al* 2014
Nam Co (Tibetan			0.1 – 1.5	0.38		Xiao *et al* 2012

plateau)						
Alert – (Canadian arctic)			0.1 – 1.5	0.8		Xiao *et al* 2012
Yukon territory Canada		40		0.86		Yu *et al* 2015

Water

TBPH has been detected in surface water close to urban areas but also in remote areas.

Venier *et al* (2014), collected water samples from 18 stations on the five Great Lakes in 2011 and 2012. TBPH was detected frequently in all the Great Lakes with the highest average concentration of 10.4 ± 1.1 pg/L in Lake Erie (n=5). The average concentration in lake Huron was 4.5 ± 1.1pg/l (n=5), in Lake Michigan 2.6 ± 0.2 pg/l (n=3), in Lake Ontario 0.27 pg/l (n=1) and in Lake Superior 3.0±0.4 pg/l (n=3).

Guo *et al* (2017), collected a total of 59 water samples, including both the dissolved and particle phases, from five tributaries to Lake Michigan in 2015. TBPH was detected in samples from all five tributaries:

Indiana Harbor and Ship Canal	Geomean	690	pg/l	(N	=	11)
Saint Joseph River	Geomean	320	pg/l	(N	=	12)
Kalamazoo River	Geomean	230	pg/l	(N	=	12)
Grand River	Geomean	430	pg/l	(N	=	11)
Lower Fox River	Geomean	83 pg/l (N = 13)				

Möller *et al* (2011a), detected TBPH in the dissolved phase of 25% of the water samples taken in the East Greenland Sea in 2009. The concentrations ranged from non-detect to 1.3 pg/l. The detection rate in the particulate phase was 6% with concentrations ranging from n.d. to 0.12 pg/L.

During a polar expedition from the east China sea to the arctic Möller *et al* (2011) TBPH was detected at one station with a concentration of 0.2 pg/l.

Sediment

There are several publications that reports findings of TBPH in sediment.

Zhu *et al* (2013) investigated the occurrence and distribution of polybrominated diphenyl ethers (PBDEs) and eleven non-PBDE halogenated flame retardants including TBPH in marine and river sediment from Yangtze River Delta, East China. TBPH was not detected in marine sediment (n=24). It was however, detected in all river sediment samples (n=6). The mean concentration was 1.01±0.38 ng/g dw (range 0.59- 7.00 ng/g dw).

La Guardia (2012) analysed TBPH in sediment and the filter-feeding bivalve (*Corbicula fluminea*) and grazing gastropod (*Elimia proxima*), collected downstream from a textile manufacturing WWTP outfall in the Yadkin River, North Carolina. The TBPH concentration in the sediment was (levels in bivalves are presented in section 7.7.3):

Outfall	19200	ng/g	TOC
16.8 km from outfall	3120	ng/g	TOC
25.2 km from outfall	3570	ng/g	TOC
44.6 km from outfall	2000 ng/g TOC		

La Guardia (2013) collected inland and coastal surficial sediments (n = 45) in August 2011 from Durban Bay and 13 rivers in the eThekwini metropolitan municipality, South Africa.

The detection rate for TBPH was 60% with a mean concentration of 96 ng/g TOC (range n.d. – 899 ng/g TOC).

Schlabach *et al* (2011) analysed sediment samples from 12 sites in the Nordic countries (Denmark 2 sites, Faroe Islands 3 sites, Finland 3 sites, Norway 1 site, Sweden 3 sites). TBPH was only detected in sediment from two sites: Torshavn (Faroe Islands) 0.23 ng/g dw and Waldemarsudde (Stockholm, Sweden) 3.3 ng/g d.w. The sediment at Waldemarsudde was sampled close to a WWTP outlet.

Olunkunle and Okonkwo (2015) collected leachate and sediment samples from six municipal solid waste landfill sites across the Gauteng Province in South Africa. TBPH was detected at two of the sites with a mean concentration of 11 ng/g dw.

Ganci *et al* (2019) collected sediment samples (n=45) in the tidal area of the river Thames over a length of 110 km from Teddington lock to the North Sea. TBPH was one of the more frequently detected Br-flame retardants with a detection frequency of 76%. The average concentration was 3.5 µg/kg dw (range <0.02-14 µg/kg dw). Based on organic carbon the average concentration was 134 µg/kg OC (range n.d-445 µg/kg OC).

Soil

Only one publication known to the evaluating Member State reports findings of TBPH in soil. KLIF (2013) detected TBPH in a pooled soil sample from Telemark (Norwegian mainland) at a concentration of 1.04 ng/g dw.

WWTP sludges

Schlabach *et al* (2011) analysed 13 sewage sludge samples from the Nordic countries (2 samples each from Denmark, Faroe Islands, Iceland, Norway, Sweden and three from Finland). TBPH was detected in all samples. The median concentration was 18 ng/g d.w and the range 3.8 – 42 ng/g d.w.

7.7.3. Bioaccumulation

Dietary studies

Bearr *et al,* 2010

Bearr *et al*, 2010 exposed Fathead minnow (*Pimephales promelas*) to Firemaster 550, Firemaster BZ-54 or DEHP via the food for 56 d with a subsequent depuration period of 22d when all fish were fed control food. Firemaster 550 is a mixture of triaryl phosphate isomers, triphenyl phosphate, and Firemaster BZ-54. Firemaster BZ-54 is a mixture of TBPH and 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB). The purpose of the study was to investigate if TBB and TBPH are bioavailable and if they adversely affect DNA integrity in fish. For the latter purpose liver and blood cells were collected and assessed for DNA damage.

The test substances were dissolved in cod liver oil and mixed into fish food. Control food included cod liver oil. Test substance concentration in the fish food is shown in

Table 12.

Table 12: Concentrations of TBPH and TBB in amended diets mean of three replicates ± standard error.

		Total (µg/g feed - wet weight)	
Feed	**% Lipid**	**TBPH**	**TBB**
Control	6.5 ± 0.3	<0.26 ± 0.014	0.20 ± 0.053
Firemaster 550	7.4 ± 0.7	744.7 ± 85.97	1658 ± 198.9
Firemaster BZ-54	7.7 ± 1.0	907 ± 166.3	2087 ± 385.0

Twenty fish held in 40 l aquaria (5 fish/aquarium) were used for each treatment and 15 for control. The fish were fed 0.2 g food/d (6% of fish body weight). The expected daily intake per fish was 150 µg TBPH and 330 µg TBB in the FM 550 feed, and 180 µg TBPH and 420 µg TBB in the BZ-54 feed. Every other day 50% of the water was exchanged 6 h after feeding. Analysis of TBPH and TBB and appearance of any metabolites was performed day 0 and day 56 on carcasses were gonads, liver and brain first had been removed.

The average length and weight of the fish at test initiation was 61±1mm and 2.42±0.21 g, respectively. After 78 d, the fish length was 67±1mm and the weight was 3.19±0.21 g.

Both TBPH and TBB concentrations in fish on day 56 were significantly higher than day 0. The highest amount of chemical measured in a single BZ-54-fed fish was 1075 ng of TBPH and 800 ng of TBB. These numbers represent 0.59 and 0.19% of the daily dosage for TBPH and TBB in the BZ-54- feed, respectively. Total recoverable TBB and TBPH were 70% less in FM 550-fed fish. However, these fish were probably not in a good condition as the survival in this treatment group was only 63% compared to 83 and 88% in the control and BZ-54 treatments, respectively. Unfortunately the information given in the publication do not allow estimation of the BMF or the depuration half-life.

During analysis of the fish tissue samples, several peaks were observed in the GC/MS chromatograms in addition to the parent compounds. The mass spectrum of these peaks suggested they were brominated metabolites of TBB. In a preliminary study, BZ-54 was incubated with active or heat killed common carp (*Cyprinus carpio*) liver microsomes for 2 h at 25°C (n=3). The concentration of TBB was 73.1±1.3% less in the active microsome samples than in the heat-killed sample while no difference (0.0±4.3%) was detected with respect to the concentration of TBPH. This suggests that TBB is rapidly metabolized in common carp microsomes, but TBPH is not.

Nacci *et al,* 2018

Nacci *et al*, 2018 investigated the uptake and depuration of TBPH in the estuarine fish, Atlantic killifish, *Fundulus heteroclitus* after dietary exposure.
Diets were amended with TBPH (TBPH_LO diet, 139 µg/g dry wt, or TBPH_HI diet, 4360 µg/g dry wt). The polychlorinated biphenyl congener 2,2',4,4'5,5' hexachlorobiphenyl (PCB153 diet, 13 µg/g dry wt), was included as a positive control for bioaccumulation.

The design was similar to OECD guideline 305 dietary bioaccumulation.
During the experimental period (42 days), fish were fed acetone amended control or contaminated diets from 0 to 28 d (uptake period), followed by a depuration period of 14 days during which time fish were fed control diet.
Wild-caught killifish (2–3 g wet wt) were kept in 38-L tanks receiving flowing seawater at a rate of 1.3 L/min. Each treatment consisted of 40 fish distributed in 10 replicate tanks, except for the PCB treatment, for which 6 tanks were used (no depuration period). Each tank contained 4 fish (2 males and 2 females). The fish were fed twice daily, and the daily feeding rate based on an average initial fish weight of 2.35g wet wt (= 0.58 g dry wt) was

approximately 15.7% based on dry weight. This gave a daily exposure of 51 µg TBPH/tank/day in the TBPH_LO diet, 1593 µg/tank/day in the TBPH_HI diet and 5 µg PCB 153/tank/day in the PCB 153 diet.

Eight fish from each treatment were sampled on day 14. On day 28 (end of uptake period) 16 fish from each treatment were sampled. Eight fish per treatment were sampled during the depuration period on days 35 and 42 of the study. Bioaccumulation of TBPH accounted for 0.46% of the total amount of chemical provided over 28 d of feeding at the lower exposure level (averaging male and female fish values; Table 13). The BMF defined as the ratio of tissue to dietary concentrations was ca 0.02. At the higher exposure level a much lower fraction of TBPH was taken up by the fish; only 0.1% of the total amount of TBPH provided via feeding was accounted for in fish and the BMF was 0.005 (mean male + female). This concentration dependence indicates reduced bioavailability with increasing exposure. Thus, the low BMFs derived in this study may not be relevant for a field situation where the exposure concentrations are much lower. The values for PCB 153 are given in Table 13 for comparison.

Time to depurate to 50% of the 28-d TBPH concentration ($T_{1/2}$) was approximately 22 d after the TBPH exposure period ended. This half-life is not growth corrected.

Table 13: BMF and substance concentrations in diet and fish

Treatment	Conc. in diet (ng/g dw)	sex	Conc in fish at day 28 (ng/g dw)	BMF	Substance accounted for in fish (%)	Conc in fish (ng/g lipid)
PCB 153 control	13	F M	24 34			
PCB 153	12 993	F M	13 115 14 883	1.01 1.15	22.93 26.02	66 677 102 372
TBPH control	25	F M	ND ND			
TBPH Low	139 000	F M	2319 3314	0.017 0.024	0.38 0.54	7748 14 089
TBPH High	4 360 000	F M	24 738 16 174	0.006 0.004	0.13 0.08	90 145 72 245

Unpublished, 2018

As a consequence of an ECHA compliance check decision the bioaccumulation potential of TBHPH was investigated in a study according to OECD Guideline 305 (Unpublished, 2018). Juvenile Rainbow trout (*Oncorhynchus mykiss*) with a weight of 2.06 ± 0.20 g and length 5.57 ± 0.15 cm at the start of the study, were used in the experiment. In total 57 fish were exposed to TBPH via the feed under flow-through conditions for a period of 28 days. The measured concentration in the feed was 652 mg TBPH/kg feed (nominal 1000 mg kg^{-1}). The exposure period was followed by a depuration phase of 28 days when the fish were fed uncontaminated feed. An equally sized control group with fish of the same age fed with uncontaminated food was run in parallel.

The TBPH exposed group and the control group were both fed at a fixed ratio of 2 % of body weight per day. Fish were held in 100 l aquaria (75 l water) with a maximum fish-to-

water loading rate of 0.1 to 1.0 g fish (wet weight) per litre of water per day. The flow rate was at least 15.6 L h^{-1}, the temperature 15 ± 2°C and the oxygen was > 60% throughout the test

Six fish per control and treatment, were sampled twice during the uptake phase (days 14 and 28) and five times during depuration (days 31.5, 35, 42, 49 and 56). Samplings were performed before the daily feeding to obtain samples from fasted fish. Weight and length were recorded before the fish were sacrificed for analytical analysis. In addition, three fish of each population were sampled for monitoring of lipid contents at the end of uptake and depuration phase.

TBPH concentrations in fish during the uptake phase ranged from 2820 µg/kg ww to 5876 µg/kg ww on day 14 (mean 3979 ± 1265 µg/kg ww), and from 4837 µg/kg ww to 11020 µg/kg ww on day 28 (mean 8583 ± 2521 µg/kg ww). Whether or not steady state was reached during the uptake phase could not be determined. During depuration, the TBPH concentrations in fish decreased slowly from a mean of 1848 ±172 µg/kg ww at the first sampling day 31.5 to 654 ± 160 µg/kg ww day 56.

Fish grew during the study and the average fish weight at the start of the test was 2.06 ±0.2 g (n=50), and after 56 days 12.1 ±1.09 in the control group (n= 6) and 10.15 ± 2.27 in the TBPH treated group. There was no statistically significant difference between treatment and control and no difference in growth rate between uptake and depuration phase.
The fish lipid content in the TBPH treated group was 5.5 ± 0.73 % (n=3) at the end of the uptake period (d 28) and 7.8 ± 0.54 % (n=3) at the end of the depuration period (d 56).

The substance was poorly absorbed and the assimilation efficiency was calculated to 0.011. The growth and lipid corrected BMF was 0.038. The depuration was slow with a growth corrected depuration rate constant of 0.015 and a growth corrected half-life of 46.2 days (see Table 14)

Table 14: BMF, depuration rate constants and half-life

	Kinetic BMF	**Depuration rate constant (d^{-1})**	**Half-life (d)**
Uncorrected	0.0048	0.044	15.6
Growth corrected*	0.0143	0.015	46.24
Growth and lipid corrected	0.0381	-	-

* Growth rate constant 0.0294

The evaluating Member State has calculated fish BCFs for TBPH using the 15 models within the OECD TG 305 BCF estimation tool using the information given in the study report. The results are presented in Figure 1.

Figure 1: Output from OECD TG 305 BCF estimation tool

Inputs

Variable	Value
Mean weight at test start (g)	2
Uptake phase duration (days)	28
Growth rate, K_g (day^{-1})	0,02937
Log K_{OW}	10,2
K_{2g} (K_2 - K_g)	0,01499
Mean fish lipid uptake end or depuration start (fraction)	0,045
Mean fish lipid depuration end (fraction)	0,075
Depuration phase duration (days)	28
BMF_{gl}	0,0381

Interim Outputs

Variable	Value
Mean weight midpoint uptake phase (g)	2,161
Mean lipid content midpoint depuration phase	0,060
K_{2gl}	0,018

Outputs

Method 1			
inputs for K1	K1	BCF Est.	Ref.
weight	433,09	24076,7	Hayton and Barron (1990)
weight	595,86	33125,5	Erickson and McKim (1990a)
weight	591,55	32885,6	Barber et al. (1991)
weight	382,32	21254,1	Barber (2003) - observed
weight	612,12	34029,2	Barber (2001)
weight	115,91	6443,9	Streit and Sire (1993)
weight	477,85	26564,8	Erickson and McKim (1990b)
weight	406,35	22590,1	Sijm et al. (1995)
weight	490,57	27272,1	Barber (2003) - calibrated
log Kow	2731,49	151850,8	Tolls and Sijm (1995)
log Kow	3015,78	167655,2	Spacie and Hamelink (1982)
weight, log Kow	105,74	5878,3	Hendriks et al. (2001)
weight, log Kow	Kow too high, set t	Inputs incomplete	Thomann (1989)

Method 2			
input	Estimated K1	BCF Est.	Ref.
K_{2gl}	603,80	33566,9	Brookes and Crooke (2012)

Method 3			
input	Estimated K1	BCF Est.	Ref.
BMF_{gl}	15,85	881,1	Inoue et al (2012)

The results indicate a BCF >5000 for all method 1 models (except 1) and for method 2 but not for method 3.

DeJourdan et al, 2014

Mesocosms with a depth of 1.2 m, a diameter of 3.9 m and were filled with water to approximately 1 m (ca 12000 L). Sediment trays 52.1 x 25.4 x 5.7 cm containing organic rich soil (OC 10% dw) were added to each mesocosm so that > 50% of bottom surface was covered. Three mesocosms were treated (2 July 2008) in triplicate with BZ-54 (a 20:80 commercial mixture of TBPH and TBB), in addition three mesocosm were used as solvent controls. The test substance was applied by subsurface injection of BZ-54 dissolved into 125mL of dimethyl sulfoxide and 5mL of toluene aiming for a concentration of 500 ng compound/g sediment in the upper 5 cm of sediment. In the solvent control an equal volume of the solvent mixture was administered to control mesocosms, representing 0.001% solvent v/v. Fathead minnow (*Pimephales promelas*) were allowed to acclimate for 10 d prior to treatment in their randomly assigned mesocosm. Minnows were contained in mesh enclosures (22 cm diameter, 40 cm long) with 12 minnows (undetermined sex, ~5 cm in length) per enclosure and 2 enclosures per mesocosm. The minnows were not fed but foraged on the zooplankton community. A plastic (10 cm x 10 cm x 5 cm) container was placed at the bottom of each enclosure and filled with the same sediment as on the bottom of the mesocosms. Samples of the water-column (~4 L) for analyses of water quality parameters (e.g. O_2, pH) were taken at -4 d, 1h, 4h, 1 d, 2 d, 4 d, 7 d, 14 d, 21 d, 28 d, 35 d, 42 d, 49 d, 56 d, and 70 d (10 September 2008) after treatment. After 42 d, fish were transferred to new mesh cages in 1 of the 3 control mesocosms for the depuration phase. Fish were sampled during the exposure period at 7 d, 14 d, 28 d, and 42 d and during the depuration period at 49 d and 70 d. On each sampling day, 3 minnows per mesocosm were randomly sampled. TBPH was only measurable in 1 fish from 1 mesocosm day 7, in 2 fish (1 from each of two mesocosms) day 14 and in 1 fish from 1 mesocosm day 28. However, the exposure in this study is unknown. Due to the limited water solubility it is assumed that the concentration in water was very low and that the fish were exposed to TBPH via the food only. The TBPH concentration in the zooplankton that the fish fed on was however not measured. This study does therefore not allow to make conclusions on the bioaccumulation of TBPH in fish.

TMF studies

Zheng *et al*, 2018 measured the concentrations of 8 novel brominated flame retardants (NFBRs) including TBPH in 17 species from Lake Taihu, South China. The food web included primary producers (seston/plankton) (n = 6), four invertebrates species including freshwater mussel (*Anodonta*) (n = 6), clam (*Lamellibranchia*) (n = 6), crayfish (*Procambarus clarkii*) (n = 6), and snail (*Bellamya purificata*) (n = 6), 12 fish species including rice field eel (*Monopterus albus*) (n = 6), blunt-snout bream (*Megalobrama amblycephala*) (n = 2), whitebait (*Hemisalanx prognathous*) (n = 5), crucian (*Carassius auratus*), carp (*Carassius cuvieri*) (n = 3), pipefish (*Tylosurus crocodilus*) (n = 3), silver fish (*Protosalanx hyalocranius*) (n = 6), whitefish (*Alburnus*) (n = 6), catfish (*Silurus asotus*) (n = 6), redfin culter (*Cultrichthys erythropterus*) (n = 7), wolffish (*Anarrhichtys Ocellaus*) (n = 3), and yellow-head catfish (*Pelteobagrus fulvidraco*) (n = 6).

The trophic level (TL) of the species was determined by stable isotope analysis. In addition, liver microsomes of crucian (trophic level [TL]: 2.93), catfish (TL: 3.86), and yellow-head catfish (TL: 4.3) were used to measure the metabolic rates of the different NFBRs. TBPH showed no significant metabolism after 24 h of incubations with the liver microsomes of the three species.

The average concentrations of TBPH in all of the sampled species was 870 ± 906 pg/g ww, and the highest concentrations (3320 ± 5730 pg/g ww) was detected in Whitefish (Table 15Table 15).

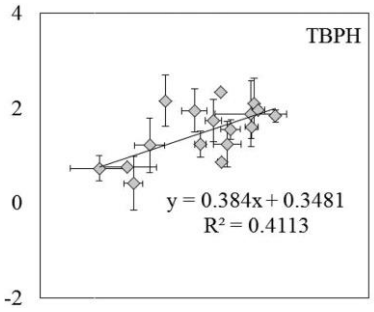
Table 15: Concentrations of TBPH in biota sampled in Lake Taihu, South China

Species	**Trophic Level**	**n**	**TBPH** (pg/g ww) mean ± SD (range)
Plankton/seston	2.00 ± 0.27	6	143 ± 90.2 (<MDL-270)
Freshwater mussel	1.08 ± 0.53	6	51.0 ± 43.8 (<MDL-43.1)
Clam	1.71 ± 0.17	6	76.2 ± 98.9 (<MDL-251)
Crayfish	1.59 ± 0.53	6	<MDL
Snail	3.16 ± 0.15	6	507 ± 445 (<MDL-1280)
Ricefield eel	2.82 ± 0.23	6	1100 ± 766 (<MDL-2540)
Blunt-snout bream	3.30 ± 0.04	2	2130 ± 101 (2050−2200)
Whitebait	2.29 ± 0.05	5	1370 ± 1850 (188−4610
Crucian	2.93 ± 0.10	6	211 ± 135 (98.7−394)
Carp	3.42 ± 0.25	3	245 ± 192 (<MDL-437)
Pipefish	3.48 ± 0.18	3	664 ± 311 (384−998)
Silver fish	3.31 ± 0.07	6	77.6 ± 6.7 (<MDL-77.4)
Whitefish	3.85 ± 0.65	6	3320 ± 5730 (<MDL-14900)
Catfish	3.86 ± 0.12	5	713 ± 480 (386−1538)
Redfin culter	3.90 ± 0.03	7	1830 ± 1450 (<MDL-4540)
Wolffish	3.99 ± 0.11	3	1040 ± 186 (897−1250)
Yellow-head catfish	4.30 ± 0.06	6	1230 ± 400 (844−1910)

A significantly positive relationship was found between trophic levels and the lipid-normalized concentration of TBPH (p = 0.004) see

Figure 2. The trophic magnification factor (TMF) was 2.42.

Figure 2: Relationship between trophic level and concentration of TBPH in biota from Lake Taihu, South China



Jin *et al* (2016), analysed brominated diphenyl ethers and NBFRs including TBPH in the livers of predatory and non-predatory birds in Korea and in addition investigated if there was a correlation between TBPH concentrations and trophic level (measured as δ5N). Ten bird species (total individuals, n = 69) were obtained from the National Science Museum in Daejeon, Korea during the period of 2010-2011. All birds were found dead from several causes, e.g. roadkill, poisoning, or starvation. Most bird samples was from the same area, Paju, Gyeonggi-do (n = 57), Of the ten species Eurasian eagle owl (*Bubo bubo*), common kestrel (*Falco tinnunculus*), collared scops owl (*Otus lempiji*), and blacktailed gull (*Larus crassirostris*) are regarded as residential predatory birds; the common buzzard (*Buteo buteo*), northern goshawk (*Accipiter gentilis*), cinereous vulture (*Aegypius monachus*), and brown hawk owl (*Ninox scutulata*) are regarded as migrant predatory birds. Oriental turtle dove (*Streptopelia orientalis*) and spotbilled duck (*Anas poecilorhyncha*) are regarded as residential herbivore and insectivore birds, respectively.

TBPH had the highest occurrence of the analysed NFBRs. The detection rate was 54%. The overall mean concentration of TBPH was 21.3 ng/g lw. The highest concentrations were found in Eurasian eagle owl and Common kestrel while the lowest concentrations were found in the non-predatory birds Spot-billed duck and Oriental turtle dove see Table 16.
The TBPH concentration was not significantly correlated with δ5N values when plotted all samples together. However, three residential and carnivorous predatory species, Eurasian eagle owl (*B. bubo*), common kestrel (*F. tinnunculus*), and collared scops owl (*O. lempiji*), showed a significant positive relationship between the concentrations of TBPH and δ15N (r2 = 0.63, p = 0.018).

Table 16: TBPH concentration in birds (liver) from Korea

Species	**Sampling location**	**N**	**Feeding habits**	**Migratory behaviour**	**TBPH in liver** ng/g lipid weight Mean (Range)	**δ15N (‰)**
Eurasian eagle owl (*Bubo bubo*)	Paju, Gyeonggi-do	5	Carnivore (pheasants, rabbits, rodents)	Resident	170 (2.24-803)	8.8 ± 1.5
Common kestrel (*Falco tinnunculus*)	Paju, Gyeonggi-do	4	Carnivore (small birds, reptiles, and insects)	Resident	52.1 (2.88-110)	7.7 ± 1.0
Collared scops owl (*Otus lempiji*)	Paju, Gyeonggi-do	6	Carnivore (insects, small birds, rodents, and crustaceans)	Resident	10.8 (<0.75-27.8)	6.5 ± 1.3

Black-tailed gull (*Larus crassirostris*)	Yeonggwang, Jeollanam-do; Ulleungdo and Dokdo islands	8	Piscivore (fish and amphibians	Resident	2.57 (<0.75-9.10)	12.9 ± 0.1
Brown hawk owl (*Ninox scutulata*)	Paju, Gyeonggi-do Gunsan, Jeollabukdo	9	Carnivore (insects, birds, rodents, and bats)	Migratory (Philippines and Indonesia in summer)	20.8 (<0.75-80.4)	5.5 ± 0.8
Northern goshawk (*Accipiter gentilis*)	Paju, Gyeonggi-do	6	Carnivore (small birds and small mammals)	Migratory (Russia, China in winter)	6.5 (<0.75-22.4)	7.9 ± 1.5
Cinereous vulture (*Aegypius monachus*)	Paju, Gyeonggi-do	7	Carnivore (mainly carrion)	Migratory (Mongolia in winter)	1.86 (<0.75-8.52)	9.5 ± 1.2
Common buzzard (*Buteo buteo*)	Paju, Gyeonggi-do	7	Carnivore (small birds and rodents)	Migratory (Russia in winter	12.2 (<0.75-63.7)	7.0 ± 0.58
Spot-billed duck (*Anas poecilorhyncha*)	Paju, Gyeonggi-do	6	Insectivore and herbivore (insects and seeds)	Resident	1.98 (<0.75-3.77)	10.0 ± 0.7
Oriental turtle dove (*Streptopelia orientalis*)	Gyeonggi-do; Gyeongsangbok-do; Jeollabok-do	11	Herbivore (nuts and seeds)	Resident	<0.75	5.9 ± 1.7

Monitoring data - Biota

TBPH has frequently been detected in biota both in rural and remote areas such as the arctic.

Sagerup *et al* (2010), analysed 14 brominated flame retardants including TBPH in the Arctic (Svalbard) 2007 - 2009. The sampled species were: Capelin (*Mallotus villosus*), Common eider (*Somateria mollissima*), Black-legged kittiwake (*Rissa tridactyla*), Brünnich's guillemot (*Uria lomvia*), Ringed seal (*Phoca hispida*), Arctic fox (*Vulpes lagopus*), Polar bear (*Ursus maritimus*). TBPH was detected in capelins, eiders, guillemots, kittiwakes and ringed seal but not in arctic fox and polar bear (see Table 17).

Table 17: TBPH in seven species from the Norwegian Arctic.

Species	**N**	**organ**	**Lipid (%)**	**Detection frequency (%)**	**TBPH** pg/g wet wt mean (standard deviation)
Capelin	10	whole	2.6	90	719 (292)
Common eider	10	Liver	3.7	60	1652 (1396)
Brünnich's guillemot	10	Egg	11.0	70	1799 (1358)
Kittiwake	10	Liver	5.5	50	800 (356)

Ringed seal	10	Liver	3.5	60	573 (198)
Arctic fox	10	Liver	7.1	Not detected	-
Polar bear	10	Plasma	0.9	Not detected	-

Schlabach *et al* (2010) report findings of TBPH in mussel, fish and birds sampled in the Nordic countries 2008-2009. TBPH was detected in 70% of the samples in concentrations between 0.002 and 0.46 ng/g w.w. The results are compiled in Table 18.

Table 18: TBPH concentrations in biota sampled in the Nordic countries 2008-2009.

Species	**Country (site)**	**Organ**	**N**	**Concentration** (ng/g ww)
Blue mussel (*Mytilus edulis*)	Iceland	-		0.009
	Norway	-	2 Composite sample	0.032 0.057
Arctic char *(Salvelinus alpinus*)	Faroe Islands	Muscle	pooled sample of 12 fish	0.011 (ng/g dw)
Perch (*Perca fluviatilis*)	Finland (Helsinki) (Tampere)	Muscle	1 pooled sample (6-10 fish)) 5 composite samples (6-10 ind/pool)	0.002 0.006 0.008 0.009 0.004 0.46
Species?	Sweden (Lake Mälaren Stockholm)	Muscle	2 pooled samples (? Fish)	<0.026 0.005
Atlantic cod (*Gadus morhua*)	Faroe Islands	Liver	1 pooled sample (20 fish)	0.2
	Iceland	Liver	1 pooled sample (25 fish)	<0.18
	Norway Åsefjorden	Liver.	3 pooled samples (5 fish)	<0.083 0.05 <0.26
Black guillemot (*Cepphus grylle*)	Faroe Islands (Skuvoy) (Koltur)	Egg	1 pooled sample (9 eggs) 1 pooled sample (10 eggs)	0.021 <0.026
Guillemot (*Uria aalge*)	Sweden (Stora Karlsö)	Egg	2 pooled samples (5 eggs)	<0.047 0.0082

KLIF 2013 reports measurements of TBPH from a screening study on the Norwegian mainland (Telemark in southern Norway and Troms, Finnmark and Lofoten in Northern Norway) and in the arctic (Svalbard). TBPH was not detected (DL 0.01 ng/g ww) in the terrestrial species sampled on the mainland: livers of Moose (n=9), Field mouse (n=8) and Shrew (n=2). It was furthermore not detected in Perch liver (n=3) but it was detected in 30% of brown trout liver samples (n=10) with a mean of 0.04 ng/g dw std dev 0.01. The screening results for marine species from the Norwegian mainland and Svalbard are shown in Table 19. It is notable that the detection frequency was 100% for Kittiwake eggs and 95% for Polar Bear plasma from Svalbard. The detection frequency of TBPH was higher on the mainland for the two species, Atlantic cod and Common eider that were sampled both on the mainland and on Svalbard.

Table 19: The percentage of samples above detection limit (DL), mean and standard deviation (in bracket) at ng/mL plasma and ng/g wet weight of samples in the marine environment (Lofoten, Troms and Finnmark, Northern Norway mainland) and in the Arctic environment (Svalbard)

Species	organ	Mainland	N	Arctic (Svalbard)	N
Mussels	Whole	N.D	3	N.A	
Atlantic cod	Liver	30% 0.14 (0.02)	10	10% 0.07	3
Polar cod		N.A	Pooled	N.D	10
Common eider	Egg	100% 0.04 (0.02)	10	58% 0.06 (0.07)	12
Herring gull	Egg	20% 1.99 (2.65)	10	N.A	
Glaucous gull	Plasma	N.A	-	17% 0.026 (0.001)	12
Kittiwake	Egg	N.A	-	100% 0.10 (0.09)	12
Harbor Seal	Liver	10% 0.10	10	N.A	
Ringed seal	Plasma	N.A	-	10% 0.04	10
Polar bear	Plasma	N.A	-	95% 0.15 (0.16)	20

In 2014 the Norwegian Institute for Water Research (NIVA) measured contaminants including TBPH in several species in the Oslo fjord (KLIF, 2014). TBPH was detected in blue mussels but not in polychaetes at three sites in the fjord (one composite sample/site). The concentrations ranged from 20 – 170 pg/g wet weight. TBPH was not detected in any other of the sampled species except for Herring gull blood (n= 15). The mean concentration was approximately 14000 pg/g lipid weight (exact value not given in the report), but the variation was high.

Klosterhaus *et al* (2012), analysed cormorant (*Phalacrocorax auritus*) eggs collected 2008 and blubber from Harbor seal (*Phoca vitulina*) stranded in 2007 - 2008 in San Francisco bay, USA. The concentrations of TBPH were below the method detection limits (12 ng/g lipid for eggs and not reported for blubber).

La Guardia *et al* (2012), analysed TBPH in sediment and the filter-feeding bivalve (*Corbicula fluminea*) and grazing gastropod (*Elimia proxima*), collected in Yadkin river, (North Carolina, USA) downstream from a textile manufacturing outfall. The TBPH concentrations are shown in Table 20.

Table 20: Concentrations in Sediments and Mollusks (*Corbicula fluminea* and *Elimia proxima*) downstream a textile manufacturing outfall.

TBPH concentration in:	**Distance from outfall**			
	outfall	16.8 km	25.2 km	44.6 km
Sediment (ng g^{-1} TOC)	19 200	3 120	3 570	2 000
Bivalve *Corbicula fluminea* (ng g^{-1} lipid)	1 370	816	nd	37
Gastropod *Elimia proxima* (ng g^{-1} lipid)	380	nd	99	36

Gentes *et al* (2012), detected TBPH in 89% (n=28) of ring-billed gull livers sampled on Deslauriers Island in the St. Lawrence river downstream from Montreal, Canada. The mean concentration was 2.16 ± 0.69 ng/g ww (range <0.04 - 17.6 ng/g ww). TBPH was not detected (DL 0.04 ng/g ww) in blood plasma samples (n=30).

Lam *et al* (2009), detected TBPH in blubber from Indo-pacific humpback dolphins (*Sousa chinensis*) (n=17) and finless porpoises (*Neophocaena phocaenoides*) (n=33) stranded in Hong Kong between 2002 and 2008. Approximately 40% (20 out of 50) of samples contained levels of TBPH above the detection limit (0.04 ng/g lw) and the majority of the detectable samples were from porpoises. The mean TBPH concentration in dolphin was 0.51 ± 1.3 ng/g lw (range <0.04 to 5.3) while the mean concentration in porpoise was 342± 883 ng/g lw (range <0.04 to 3859) respectively.

Zhu *et al* (2014), investigated levels of polybrominated diphenyl ethers (PBDE) and five PBDE alternatives including TBPH in blubber of finless porpoise (n=38) and Indo-Pacific humpback dolphin (n=23). The blubber was sampled from animals stranded in Hong Kong between 2003 and 2012. TBPH was detected in over 80% of porpoise samples at concentrations ranging from < 0.02 to 1.06 ng/g lw, mean 0.098 ± 0.169. In dolphins the detection frequency was 83%, the concentration range was < 0.02 to 7.55 ng/g lw and the mean concentration was 0.517 ± 1.54 ng/g lw.

Vorkamp *et al* (2015), analysed biota samples collected in Central East Greenland in 2012, and included black guillemot (*Cepphus grylle*) eggs (N = 3), glaucous gull (*Larus hyperboreus*) liver (N = 4), blubber of ringed seal (*Pusa hispida*) (N = 5) with additional ringed seal samples from West Greenland (N = 4), and polar bear (*Ursus maritimus*) adipose tissue (N = 5). The overall detection frequency was 24%. TBPH was not detected in Glaucous gull or ringed seal. It was however detected in all three samples of Black guillemot eggs and in three of five samples of bear adipose tissue with a mean and (range) of 0.061 (0.050-0.066) ng/g ww and 0.26 (<0.128 – 0.402) ng/g ww, respectively.

Guerra *et al* (2012) compared the concentrations of brominated flame retardants in peregrine falcons eggs (*Falco peregrinus*) collected (2007–2009), in Canadian Great Lakes–St. Lawrence River and the province of New Brunswick in eastern Canada (N= 12) and eggs collected in Guadalajara and Bilbao, Spain 2003- 2006 (N= 13). TBPH concentrations were detected in 1 peregrine egg from coastal Bilbao, Spain in a concentration of 1.2 ng/g lw and in 4 eggs from Toronto (N= 2) and Montreal (N= 2), Canada with a mean concentration of 2.1 ng/g lw (range 1.1 – 4.5 ng/g lw).

Lazarus *et al* (2016) reports findings of TBPH in Osprey (*Pandion Halietus*) sampled in tributaries to the Chesapeake Bay, USA between 2011 and 2013. TBPH was detected in 3 of 12 eggs from Poplar Island (<MDL–31.3 ng/g ww), 3 of 10 eggs from Susquehanna river (<MDL–2.4 ng/g ww), 3 of 13 eggs from Anacostia and Potomac rivers (<MDL–7.4 ng/g ww), 1 of 12 eggs from James river (<MDL–0.54 ng/g ww) and 2 of 4 eggs from Back river (<MDL–4.3 ng/g ww)

Fernie *et al* (2017) analysed blood plasma from peregrine falcons (Falco peregrinus) sampled across the Canadian Great Lakes-St. Lawrence River Basin in 2010. TBPH was detected in 43 % of falcons from urban regions. The arithmetic mean concentration was 1.18±0.5 ng/g ww (range ND-9.57). The detection frequency in falcons from rural regions was 40%. The arithmetic mean TBPH concentration was 8.0±0.2 ng/g ww (range ND-98.3).

Terrestrial bioaccumulation

With a log Kow of 10.5 and a log Koa of 15.4 (Koawin v1.10) TBPH fulfils the screening criteria for terrestrial bioaccumulation (log Kow >2 and log Koa >5). No studies on bioaccumulation in terrestrial species are available. The available toxicokinetic data (see section 7.9.1) indicate that TBPH is poorly absorbed and poorly metabolised and is mainly excreted unchanged via faeces. This is what can be expected for such a large substance (MW=706) with a log KOW >10. However, a small fraction of the substance seems to be accumulating in tissues of the exposed organisms. Studies of repeated oral exposures showed that while only a small amount of TBPH is absorbed, it has the potential to accumulate in adrenal and liver tissue, largely as the parent substance. This is apparent from the available monitoring data that suggests that TBPH accumulates in air breathing animals. TBPH has been detected in liver and eggs from several bird species including raptors preying on terrestrial species as well as birds that feed on aquatic organisms also in the Arctic. It is not possible to derive BMF values for the different bird species from these monitoring studies as the concentrations in their feed is not known. Furthermore, TBPH has been detected in blubber from marine mammals such as finless porpoise and dolphins and in the liver of the arctic species ringed seal and in the plasma of polar bears. To conclude, TBPH is present in a wide range of air breathing birds and mammals including top predators both in more industrialised areas as well as in remote regions, such as the Arctic. In addition, TBPH has been detected in plasma and breast milk of nursing women. He *et al* (2013) analysed serum from 305 residents in the Laizhou bay area in China. The samples were pooled in 10 groups (5 age groups per gender: 20-29, 30-39, 40-49, 50-59 and >60). TBPH was detected in females in the age group 30-39 years at a concentration of 260 ng/g lw. but not in the other four female age groups and not in males. Zhou *et al* (2014) analysed several brominated flame retardants including TBPH in paired human maternal serum (n=102) and breast milk (n=105) collected in the Sherbrooke region in Canada 2008-2009. The detection frequency for TBPH in serum was 16.7% (LOD 7.3 ng/g lw) and in milk 32.4% (LOD 0.15 ng/g lw). The concentrations in serum ranged from ND to 164 ng/g lw and in milk from ND to 6.6 ng/g lw.

Summary/discussion

Three dietary bioaccumulation studies are available. Only a small part of the total given doses is found in the fish at the end of the exposure period in all three studies. This is probably due to that TBPH is poorly absorbed in the gut of the fish and not because of metabolism and excretion. No difference (0.0±4.3%) was detected with respect to the concentration of TBPH incubated with active or heat killed common carp (*Cyprinus carpio*) liver microsomes for 2 h at 25°C (n=3). BMFs were measured in two of the studies (Nacci, 2018 and Unpublished, 2018) and the BMFs were low and of similar magnitude in both studies. Comparing these BMFs (Table 21) with the finding by Inoue *et al* (2012) that a BMF (growth-corrected and lipid-normalised) above 0.31 corresponds to a BCF (lipid normalised) over 5,000 L/kg would suggest that TBPH is not vB according to the REACH Annex XIII criterion. However, the TBPH concentration in the food was very high in both studies and may have led to reduced bioavailability and as a consequence underestimated

the BMF value. This is supported by the fact that the BMF at the high dose in the Nacci study was 4 times lower than in the low dose. The TBPH concentration in the food in the unpublished study was comparable to the high dose of the Nacci study. It is therefore plausible that the unpublished study has underestimated the BMF to some extent. What the growth and lipid corrected BMF in the Nacci study would be is not possible to calculate from the information given in the published paper.

Contrary to this all 15 models within the OECD TG 305 BCF estimation tool except 1 (method 3) which builds on the findings by Inoue predicts BCFs> 5000 (see Figure 1). All models in method 1 and 2 are based on a predicted uptake rate constant. Considering the low uptake seen in the bioaccumulation studies these methods probably overestimate the uptake rate and thus overestimate the BCF of TBPH. It is also noted that the log Kow of TBPH is higher than the applicability domain of all three methods which according to OECD guidance document 264 (OECD, 2017) is approx. 3.5 – 8.3 for method 1, approx. 3 – 8.2 for method 2 and approx. 4.3 – 9. Furthermore, method 3 was developed from data on Carp (*Cyprinus* carpio) and the applicability for other species is unknown. On the other hand, TBPH does not seem to be metabolised by fish and the depuration rate is slow. Brooke and Crookes, 2012 suggests that a K_2 of 0.085 equals - BCF 5000 and a K_2 of 0.178 equals BCF 2000. Comparing the non-corrected depuration rate constants (Table 21) from the two studies with these values suggests that TBPH is very bioaccumulating. Furthermore, the only TMF study known to the evaluating Member State where a TMF of 2.42 for TBPH was derived (Zheng *et al*, 2018), gives support to such a conclusion. In addition, Jin *et al* (2016) found a correlation between trophic level and TBPH concentration in resident birds of Korea. To this can be added numerous findings of TBH in biota including Arctic species such as ringed seal and polar bear. In addition, toxicokinetic studies indicate that despite a low uptake a small fraction of the substance seems to accumulate in tissues (especially adrenal and liver tissue) of the exposed animals. TBPH has also been detected in placentas of rats exposed to TBPH during gestation. Furthermore, TBPH has been detected in plasma and milk of nursing mothers. Therefore, based on all available information the evaluating Member State considers TBPH to fulfil the criteria for being very bioaccumulating according to the criteria in REACH Annex XIII.

Table 21: BMF, depuration rate constants and depuration half-lives from the dietary bioaccumulation studies by Nacci (2018) and Unpublished (2018)

	BMF (conc in fish/conc in diet)	**Depuration rate constant, K2** (day -1)	**Depuration half-life** (d)
Nacci (2018)			
High dose	0.005*	0.031*	22*
Low dose	0.02*	0.031*	22*
Unpublished (2018)			
	0.0048*	0.044*	15.6*
Growth corrected	0.0143	0.015	46.2
Growth and lipid corrected	0.0381	-	-

* not growth or lipid corrected

7.8. Environmental hazard assessment

7.8.1. Aquatic compartment (including sediment)

7.8.1.1. Fish

Short term toxicity

A short-term toxicity study according to OECD TG 2003 is available in the registration dossier. The test substance Pyronil 45 had a purity > 95% but is stated to have more impurities than the registered substance. The test species was Rainbow trout (*Onchorhynchus mykiss*) with a mean weight of 1.45 g. The nominal test concentrations were: 62.5, 125, 250, 500, 1000mg/L Analytical monitoring was performed at 0 and 96 h. Undissolved material was observed in all dosed vessels the mean measured concentrations at 0 hours were: 3.7, 9.9, 30.7, 28.6, 30.4 mg/L and at 96 hours: 2.59, 1.57, 0.637, 2.65, 0.922 mg/L.

No effects were observed at any of the test concentrations and thus the NOEC was higher than the solubility of TBPH in the test medium.

Long term toxicity

Long term studies have been waived by the registrant.

Studies from the open literature

McGee *et al*., 2013, investigated effects in developing zebrafish embryos (*Danio rerio*). TBPH was tested at concentrations in the range from 0.1 to 10 µM (= 0.071-7.01 mg/L) from 5.3 to 96 Hours post fertilisation (hpf) (= 24 hours post hatch). TBPH did not cause any significant effects on embryonic survival or development at the tested doses.

Saunders *et al* (2015) performed a 21-day short term fish fecundity assay with Japanese medaka (*Oryzias latipes*) to investigate if a mixture of TBPH and TBB affect endocrine function in vivo. Medaka were fed either a high dose diet (TBPH 1422 + TBB 1474 µg/g food w/w) or a low dose (TBPH 138 + TBB 144 µg/g food). Cumulative production of eggs was used as a measure of fecundity and abundances of transcripts of 34 genes along the hypothalamus–pituitary–gonadal–liver (HPGL) axis were quantified to determine mechanisms of observed effects.

Neither the low dose nor the high dose TBPH/TBB mixture did affect the hepato-somatic or the gonado-somatic index of the fish compared to the control. The proportion of eggs that were fertilized was determined on days 7, 14, and 21. There were no differences in fertility between groups of medaka exposed to the control diet and medaka exposed to the TBPH/TBB mixtures. The low dose did not impair fecundity (egg production 94% of control) while the cumulative fecundity was significantly impaired in medaka exposed to the high dose mixture (egg production 68% of control).

Abundances of transcripts of genes of the HPGL axis were quantified in male and female medaka exposed to the high dose mixture. A pattern of global downregulation of gene transcription at all levels of the HPGL axis was observed, but effects were sex specific. In female medaka the abundance of transcripts of ERβ was lesser in livers, while abundances of transcripts of VTG II and CHG H were greater. In male medaka, abundances of transcripts of ERα, ERβ, and ARα were lesser in gonads and abundances of transcripts of ERβ and ARα were lesser in brain. Abundances of transcripts of genes encoding proteins for synthesis of cholesterol (HMGR), transport of cholesterol (HDLR), and sex hormone steroidogenesis (CYP 17 and 3β-HSD) were significantly lesser in male medaka, which might have implications for concentrations of sex hormones. The results of this study indicate that a mixture of TBPH and TBB has the potential to impair the reproductive axis

of fishes. The study gives however, no information on the relative importance of the two substances for the effects seen.

Bearr *et al*, 2010 exposed Fathead minnow (*Pimephales promelas*) to Firemaster 550 (mixture of triaryl phosphate isomers, triphenyl phosphate, and Firemaster BZ-54), Firemaster BZ-54 (TBPH and TBB).or DEHP via the food for 56 d with a subsequent depuration period of 22d when all fish were fed control food (Exposure levels shown in

Table 12). The purpose of the study was to investigate if TBB and TBPH are bioavailable and if they adversely affect DNA integrity in fish. For the latter purpose liver and blood cells were collected day 14, 28, 56 and 78 and assessed for DNA damage using the Comet assay. The exposure to Firemaster 550 or Firemaster BZ 54 did not cause any lethality or effects on growth and did not significantly induce DNA damage in blood cells above respective control levels. However, BZ 54 exhibited a statistically significant increase in percent tail DNA on days 28 (3.4 times greater than controls) and 56 (6.3 times greater). Elevated DNA damage levels were not observed after 22 d of recovery. Fish exposed to FM 550 exhibited significant increases in percent tail DNA at all 3 exposure time points. The differences between the treatment and the controls increased from 1.8 times greater at day 14, 3.0 times greater than controls at day 28, and 5.8 times greater than controls at day 56.

7.8.1.2. Aquatic invertebrates

Short term toxicity

Short term studies have been waived because a long-term study is available.

Long term toxicity

The registration dossier contains a semi-static 21 d *Daphnia magna* Reproduction Test (OECD TG 211). The study was a limit test with a nominal test concentration of 1 mg TBPH/L. No toxic effects were observed at the nominal test concentration of 1 mg/L which according to the robust study summary corresponded to a measured concentration of < 0.0334 mg/L. Thus, the NOEC was higher than the maximum water solubility of TBPH in the test medium (NOEC > WS).

7.8.1.3. Algae and aquatic plants

An algae study performed according to OECD TG 201 using the green algae *Desmodesmus subspicatus* is available. The study was a limit test with a nominal test concentration of 100 mg TBPH/L. No toxic effects were observed at the tested concentration which according to the robust study summary corresponded to a measured concentration of < 0.0334 mg/L. Thus, the NOEC was higher than the maximum water solubility of TBPH in the test medium (NOEC > WS).

7.8.1.4. Sediment organisms

No studies.

7.8.1.5. Other aquatic organisms

No studies

7.8.2. Terrestrial compartment

The registrant has waived terrestrial toxicity studies with the argument that direct and indirect exposure of the soil compartment is unlikely.

Studies from the open literature

The evaluating Member State has found two studies on effects of TBPH exposure on birds.

Egloff *et al*., 2011, investigated in vitro effects (cell viability and mRNA expression) of TBPH in primary cultures of chicken embryonic hepatocytes (CEH). TBPH did not affect hepatocyte viability at any of the administered concentrations (CEH: 0.001–30 M) and it did not affect the mRNA expression of any of the genes of interest in CEH.

Guigueno *et al.* (2018) injected fertilised eggs of American kestrel (*Falco sparverius*) on embryonic day 5 into the air cell with either organic safflower oil only or 1 of 3 fixed doses (13, 64, or 116 ng/g egg) of TBPH (>99% purity). At embryonic day 12, a subset of 3 eggs were collected from the control group and 3 eggs from the high dose of TBPH to determine in ovo concentrations, and hence embryonic exposure. The in ovo concentrations ranged between 1.4-2.5 ng/g ww.
Embryos hatched at approximately embryonic day 28. Brains were removed from 6–8 hatchlings per group and the volumes of the hippocampus and telencephalon and volumetric differences between left and right hemispheres were measured. There was evidence for a sex-specific effect of TBPH on the mean hippocampus volume of female; hatchlings in the high dose group had significantly enlarged hippocampus compared to control. No other effects were seen in the study. The authors speculate that that the altered hippocampus volume may have the potential to affect spatial memory relating to ecologically relevant behaviour such as prey capture, predator avoidance, and migration.

7.8.3. Microbiological activity in sewage treatment systems

The registration contains an activated sludge, respiration inhibition test (OECD Guideline 209). The nominal test concentrations were: 10, 100, and 1000 mg/L. No analytical monitoring was performed. The substance showed 0% respiration inhibition of activated sludge within the test. The 3h NOEC > WS.

7.8.4. PNEC derivation and other hazard conclusions

No effects of TPBPH were observed in any of the aquatic tests performed i.e. TBPH showed no effects up to its water solubility limit. A relevant PNEC can therefore not be calculated. However, effects on subcellular levels have been observed in fish simultaneously exposed to TBPH and TBB in high doses. The significance of these findings is unclear and whether or not TBPH contributes to the effects seen is not known.

No studies on terrestrial species are available except for an in vitro study on chicken embryonic hepatocytes in which no effects were seen and an in ovo study on American kestrel where a sex specific effect on hippocampus volume in female hatchlings were seen.

Table 22:

PNEC DERIVATION AND OTHER HAZARD CONCLUSIONS		
Hazard assessment conclusion for the environment compartment	**Hazard conclusion**	**Remarks/Justification**
Freshwater	PNEC > water solubility No effects up to the limit of water solubility.	
Marine water	No effects up to the limit of water solubility in freshwater. No studies on marine species available.	
Sediments (freshwater)	No effects up to the limit of water solubility in freshwater. No studies on sediment dwelling organisms available.	
Sediments (marine water)	No effects up to the limit of water solubility in freshwater. No studies on marine sediment dwelling organisms available.	

Sewage treatment plant	No effects up to the highest tested dose 1000 mg/L	

7.8.5. Conclusions for classification and labelling

No classification

7.9. Human Health hazard assessment

7.9.1. Toxicokinetics

The *in vitro* and *in vivo* data indicate that TBPH is poorly absorbed or metabolised and is mainly excreted unchanged via feces. However, a small fraction of the substance is absorbed and accumulate in tissues of the exposed organisms.

7.9.1.1. *In vitro* data

Metabolism of TBPH has been studied *in vitro*, using human and rat liver and intestinal subcellular fractions (Roberts *et al*., 2012). In experiments with human liver microsomes a significant loss of TBPH was not observed and no metabolites were detected. Mono(2-ethylhexyl) tetrabromophthalate (TBMEHP), a hydrolysis metabolite of TBPH was slowly formed when porcine hepatic carboxylesterase was added to the assay. In a previous study, metabolism of DEHP to its toxic metabolite mono(2-ethylhexyl) phthalate (MEHP) was measured to be at a rate approximately 100 times faster than the hydrolysis of TBPH to TBMEHP (Niino *et al*., 2003).

7.9.1.2. *In vivo* data

In vivo, metabolism of TBPH was studied in female rats exposed to the flame retardant Uniplex FRP-45 (Silva *et al*., 2015). Animals were administrated 500 mg/kg Uniplex FRP-45 (>95% TBPH) by gavage. No TBPH or oxidative metabolites similar to those formed by DEHP were found in serum or urine after 24h. Tetrabromo phthalic acid (TBPA) was identified as a urinary and serum metabolite at low levels. The mean urinary levels were ca. 0,5 mg/L and mean serum levels ca. 0,05 mg/L. Tetrabromobenzoic acid (TBBA), the metabolite of 2-ethylhexyl tetrabromobenzoate (TBB) was detected at concentrations much higher (ca. 100 times in urine and ca 25 times in serum) than TBPA, even though TBB was only a minor constituent (< 5%) in the mixture. The study authors hypothesized that because of its relatively low solubility and high molecular weight, TBPH may be excreted unchanged via feces.

A study was conducted in rats and mice (Knudsen *et al*., 2017). A single dose of 14C-labeled TBPH was administered to female Sprague Dawley rats by gavage at 0.1 or 10 µmol/kg (N= 4/dose group) to examine dose effects. Male mice (B6C3F1/Tac) were dosed a single gavage dose of 0.1 µmol/kg. To determine the fate of systemically available TBPH, a single intravenous (IV) bolus (0.1 µmol/kg) was injected into the lateral tail vein of female rats. Bioaccumulation potential in female SD rats was assessed by examining [14C]-radioactivity recoveries in excreta and tissues collected 24 h after 10 daily oral administrations of BEH-TEBP (0.1 µmol/kg, N=4).

In rats approximately 75% of the administered dose was recovered in faeces and less than 0.3% in urine after 24 h, with negligible difference between the doses. After 72 h rats had eliminated 92–98% of TBPH unchanged in faeces and 0.8–1% in urine. [14C]-radioactivity retained in tissues collected at 72 h following oral administration was low (~1% of total dose in assayed tissues). The disposition of TBPH in male mice and female rats was similar.

Recovery 72 h after IV administration reached 78% in faeces and 1.3% in urine. About 20% of the IV-administered TBPH was retained in tissues with 7% in liver, 5% in muscle, 3% in skin, 2% in fat and 1% in the adrenal gland. Faeces collected after IV dosing appeared to contain a mixture of parent (~30%) and metabolites (TBMEHP~70%).

Similar to a single dose, repeated administration of TBPH resulted in a small amount of the total dose excreted in urine and the majority in faeces. Total elimination was determined at 24 h intervals and compared to elimination from animals administered a single dose. Bioaccumulation was observed in liver and adrenals following 10 daily oral administrations. Significantly more TBPH was present in liver after 10 doses (113±16 pmol-eq/g) than after one (23±4 pmol-eq/g). Concentrations in adrenal tissue increased more than 10-fold after 10 doses (see Table 23).

Table 23: [14C]-radioactivity in selected tissues of rats 24 hours following a single oral dose of TBPH (0.1 µmol/kg) or 24 hours after the final dose of 10 repeated oral doses of 0.1 µmol/kg /day

Tissue	**Dose recovered** (%)		**Concentration** (pmol-eq/g)	
	1 dose	10 doses	1 dose	10 doses
Feces	91 ± 11	100 ± 5	-	-
Urine	0,3 ± 0.1	0,6 ± 0.1	-	-
Adipose	0,3 ± 0.1	0,6 ± 0.1	4 ± 5	8 ± 7
Adrenal	0.4 ± 1	0.04 ± 0.1	20 ± 5	207 ± 142
Kidney	0.01 ± 0.003	0.01 ± 0.004	1 ± 1	3 ± 1
Liver	0.01± 0.01	0.002 ± 0.001	23 ± 4	113 ± 16
Skin	1 ± 0.2	0.4 ± 0.09	1 ± 1	3 ± 1

The results of this study indicated poor absorption of TBPH after gavage administration. Studies of repeated oral exposures showed that while only a small amount of TBPH is absorbed, it has the potential to accumulate in adrenal and liver tissue, largely as the parent substance.

Baldwin *et al*. (2017) exposed Wistar rats (N=24) to FM 550 for 10 days during gestation (GD 9-18). The rats were exposed to either 0 µg, 300 µg or 1000 µg FM 550 via the feed producing exposures of approximately 0, 1 and 3.3 mg/kg bw per day. FM 550 is a TBPH/TBB/Organophosphate mixture with the ratio TBPH+TBB: organophosphates - 50:50. The TBPH:TBB ratio in the mixture is approx. 20-30:70-80. Based on these relationships the TBPH exposure in the low and high dose can be calculated to approx. 30-40µg (0.1 mg/kg bw/dy) and 100 – 130 µg (0.33 mg/kg bw/day), respectively.

The rats were sacrificed on GD 18, four hours after final dosing. TBPH, TBB, and organophosphates were analysed in homogenized whole placenta (6 per sex per group). The TBPH:TBB ratio in the placentas was similar to the TBPH:TBB ratio in FM 550. The results excluding the organophosphates are presented in Table 24.

Table 24: Concentration of TBPH and TBB in placenta associated to male or female fetuses of rats exposed to the flame retardant formulation FM 550.

	Substance	Exposure FM 550 (mg/kg bw per day)					
		0		1		3.3	
		♂	♀	♂	♀	♂	♀
Concentration in placenta (ng/g ww)	**TBPH**	N.D	N.D	10.8 ± 1.2	8.9 ± 0.5	31.5 ± 2.4	26.8 ± 1.3
	TBB	N.D	N.D	25.3 ± 4.8	21.2 ± 3.6	86.1 ± 15.9	105.5 ± 12.5

7.9.2. Acute toxicity and Corrosion/Irritation

Not assessed.

7.9.3. Sensitisation

Not assessed.

7.9.4. Repeated dose toxicity

7.9.4.1. Sub-acute toxicity

In a 28-day study, rats were treated with ca 22, 223 or 2331 mg/kg bw/day TBPH via diet . Also, five males and five females treated with 1507 mg/kg bw/day DEHP were included in the study as positive control.
In animals treated with TBPH slightly lower body weight gain (not statistically significant) was reported in females at the high dose. Perturbations in clinical chemistry parameters, including reduced alanine amino-transferase activity was also reported at the high dose. No organ weight or histopathology changes were observed.
In the animals treated with DEHP decreased body weight gain, changes in blood chemistry, markedly higher liver weights, lower testes weight and testes histopathological changes were observed.
Taken together, the result of this study is consistent with other observations indicating that the substance causes minimal toxicity. Nevertheless, presence of some toxicity indicates that small levels are absorbed and can cause systemic effects.

7.9.4.2. Sub-chronic toxicity

A reliable 90-day study with TBPH performed according to the OECD TG 408 is available . Rats were treated by gavage with 100, 300 or 1000 mg/kg bw/day in arachis oil as vehicle. No treatment-related effects were reported up to the highest dose.

7.9.5. Mutagenicity

Genotoxicity studies indicate that TBPH is not mutagenic in bacteria or mammalian cells but induces chromosomal aberrations *in vitro*. However, the substance does not seem to be clastogenic *in vivo*. TBPH did not induce mouse micronuclei formation in the available erythrocyte micronucleus test. Limited genetic toxicity data are available for other brominated phthalates.

7.9.5.1. *In vitro* genotoxicity

In the registration two negative Ames tests, according to the OECD TG 471 with the substance are provided (from 1987 and 2017). Also, a negative *in vitro* Mammalian Cell Gene Mutation test according to the OECD TG 476 (2013) is available indicating that the substance does not induce point mutations.
An *in vitro* Chromosome aberration test (OECD TG 473) with TBPH showed a statistically significant increase in aberrant cell frequencies at the highest dose (1987). The result indicated weak clastogenic activity *in vitro*.

7.9.5.2. *In vivo* genotoxicity

An *in vivo* mammalian erythrocyte micronucleus test (OECD TG 474) with the substance (purity >95%) is available (1987). The study was performed in mouse, via two exposure routes, i) a single intraperitoneal administration and ii) dermal route for five days. No treatment related increase in the number of micronuclei was reported and the test was concluded negative for cytogenicity.

7.9.6. Carcinogenicity

Not assessed.

A report is available in which a category approach was applied to 67 brominated flame retardants, including bis(2-ethylhexyl) tetrabromophthalate (Wedebye *et al*., 2016). Based on structural similarity the substances were divided into 15 groups. Bis(2-ethylhexyl) tetrabromophthalate was assigned to the group of "Phthalates/benzoates" together with TBB (CAS 183658-27-7), TBPA-diol (CAS 20566-35-2) and Bis(methyl)tetrabromophthalate (CAS 55481-60-2). (Q)SAR predictions for a number of environmental and health effects within these initial groups were generated and investigated. All members were predicted to be persistent and to have positive indications for carcinogenicity and weak genotoxicity.

7.9.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

7.9.7.1. Fertility

No reproductive toxicity study with TBPH is available.
Studies are available with the fire-retardant products consisting of TBPH in mixture with other substances.

A reproductive toxicity study with the fire-retardant product, Firemaster 550 is available (Patisaul *et al*., 2013). FM 550 contains four components: Triphenyl phosphate (TPP), a mixture of isopropylated triphenylphosphate isomers (ITPs), ethylhexyl-tetrabromobenzoate (TBB) and TBPH. Rats were exposed by the oral route to 100 or 1000 µg/day across gestation and lactation.

Data showed disruption of the thyroid hormone system in the dams. The total serum thyroxine (T4) level was dose-dependently elevated in dams with statistical significance at the high dose, whereas there was a decrease in T4 in pups. Serum triiodothyronine (T3) levels in dams were decreased without statistical significance. It is unclear why T4 levels increased. No effects on hepatic deiodinase activity were observed, suggesting the increase in T4 was not due to inhibition of outer ring deiodination. There is no evidence that TBB or TBPH inhibit the activity of conjugating systems responsible for clearing T4 from the body. In the pups in both sexes the most distinctive effect was markedly increased body weight. In the male offspring significantly increased body weight was observed on PND 10 and persisted through weaning on PND21. In female pups body weight increase was reported on PND21 (51,6 compared to 39,4 in controls). In female pups, pubertal onset was

significantly advanced at the high-dose and was associated with elevated body weights. Increased body weight is a contributing factor, but hormonally active compounds may also play a role for early pubertal onset in girls as reported previously (Patisaul *et al*., 2013). FM550 is of concern because it appears to be both obesogenic and endocrine disrupting, suggesting that it may be contributing to early puberty via multiple mechanisms.
The behavioural testing data suggested sex-specific effects on exploratory and anxiety-related behaviour.

FM 550 components accumulated in tissues of exposed dams and offspring and induced phenotypic hallmarks associated with metabolic syndrome in the offspring. Effects included increased serum thyroxine levels and reduced hepatic carboxylesterase activity in dams and advanced female puberty, weight gain, male cardiac hypertrophy and altered exploratory behaviours in offspring. Results of this study implicate FM 550 as a potential endocrine disruptor and an obesogen.

The study authors concluded that uncertainty of using these data to characterize the hazard for TBPH or TBB lies in the attribution of the toxicity observed to either mixture component. Limited toxicity studies with TBPH or TBB alone are available. Given that the metabolites of TBPH and TBB are different, it is expected that any toxicity observed would not be by the same mode of action. Therefore, the data on the potential for TBPH to cause reproductive/developmental toxicity is not conclusive.

7.9.7.2. Development

The registration dossier contains a prenatal developmental toxicity study (OECD TG 414) with TBPH. Pregnant rats were dosed by gavage on gestation days 5-19 with 250, 500 or 1000 mg/kg bw/day. No treatment related changes in dams or offspring were reported.

7.9.8. Hazard assessment of physico-chemical properties

Not assessed.

7.9.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

In the registration no DNELs for acute toxicity or for local effects are derived.

The DNELs for long-term systemic toxicity are based on NOAEL=1000 mg/kg bw/d from the available repeated toxicity studies, performed via oral (gavage) route.

7.9.10. Conclusions of the human health hazard assessment and related classification and labelling

The substance is self-classified as Eye Irrit. 2. No other classification is warranted based on the currently available information.

7.10. Assessment of endocrine disrupting (ED) properties

The scope of the ED evaluation was for the environment and human health. In the registration(s) an assessment of the potential ED properties for the ENV and HH has been provided (update 2019).

7.10.1. Endocrine disruption – Environment

The in vitro data are evaluated in section 7.10.2.1. The evaluating Member State has not located any in vivo studies on TBPH itself relevant for environmental ED assessment. However, one study on fish with simultaneous exposure to high concentrations of TBPH

and TBB is available (Bearr *et al.*, 2010, see section 7.8.1.1 above). In this study on Japanese medaka a pattern of global downregulation of gene transcription at all levels of the HPGL axis was observed. These effects were sex specific. TBB is more bioavailable than TBPH and is metabolised to a large extent while TBPH seems not to be metabolised by fish. It is therefore probable that the effects seen in these studies to a large extent are due to the exposure of TBB.

7.10.2. Endocrine disruption - Human health

A concern for endocrine disrupting properties of TBPH was identified based on:

(i) read-across to the analogue substance bis(2-ethylhexyl) phthalate (DEHP) and
(ii) data on fire retardant products containing mixtures of TBPH and other brominated substances.

The analogue phthalate DEHP is an endocrine disruptor for human health and environment and listed on annex XIV of the REACH regulation. DEHP has been shown to act as an androgen agonist and cause reproductive toxicity. Developmental toxicity studies show that DEHP alters sexual function and development in mice and rat. Also, possible effects on thyroid system were reported.
Structural analogy to DEHP suggests potential for ED activity and reproductive toxicity for TBPH. However, there is limited evidence that debromination of TBPH (or other brominated phthalates) occurs. There is evidence that under laboratory conditions debromination can occur, as shown in a photolysis study by Davis and Stapleton 2009. However, *in vivo* data indicate that TBPH is not debrominated or metabolised to DEHP.

7.10.2.1. *In vitro* data

The ED potential of three brominated flame retardants: TBPH, tetrabromocyclooctane (TBCO) and ethylhexyl-tetrabromobenzoate (TBB) was studied *in vitro* using the yeast YES/YAS reporter assay and the mammalian H295R steroidogenesis assay (Saunders *et al*., 2013).
In this study TBPH and TBCO produced anti-androgenic effect, while TBB produced an anti-estrogenic effect in the yeast assay. Significant effects were also observed in the H295R assay suggesting that the three compounds target the biosynthetic pathway of E2. TBB, TBPH and TBCO resulted in a 2.8-, 5.4- and 3.3-fold increase in concentrations of E2, respectively. TBPH exposure resulted in the greatest increase in E2, though only TBCO showed as a dose-dependent increase. Further, data from the YES assay suggested that these substances do not interact with the estrogen receptor in an agonistic fashion. This is consistent with what has been shown with MEHP (metabolite of DEHP) that affects aromatase activity.

In another study TBPH was investigated using a yeast reporter gene assay to determine possible hormonal activity. No (anti)estrogenic or (anti)androgenic activity was reported (Ezechiaš *et al*., 2012).

In another study the effect of TBPH, TBB and TBCO on steroidogenesis was investigated using a porcine primary testicular cell model (Mankidy *et al*., 2014). In this assay sex hormone production in a mixed population of human testicular cells was examined. Simultaneous measurements of steroids and gene expression of regulatory enzymes provide insight into the effects on steroidogenesis.
Following exposure to TBCO and TBPH greater production of testosterone (T) and estradiol (E2) was observed. TBB did not affect sex-steroid production. Induced gene expression of CYP11A in TBPH exposed cells and CYP17A in TBCO exposed cells indicated that effects on hormone production may be mediated by regulation of these molecular targets in the steroidogenesis pathway. Also, expression of CYP19A1, which catalyses conversion of T to E2 was significantly increased at the highest concentration of TBPH (15 mg/L). These data are in agreement with the previous report using the H295R cell system (Saunders *et al*., 2013).

In another study the potential anti-androgenic, anti-thyroid and anti-glucocorticoid activities of TBB and TBPH and their metabolites TBBA and TBMEPH were compared using a luciferase reporter gene assay (Klopcic *et al*., 2016).
All four compounds showed anti-androgenic and anti-thyroid activities, without agonist activities on the respective receptors. Anti-androgenic activities with IC50 values of 43.5 mM, 0.1 mM, 47.5 mM and 1.3 mM were reported for TBB, TBPH, TBBA and TBMEPH, respectively. The anti-thyroid hormonal IC50 values were 37.5 mM, 0.1 mM, 22.8 mM and 32.3 mM for TBB, TBPH, TBBA and TBMEPH. Further, the parent compounds exhibited anti-glucocorticoid activity by direct competing to the glucocorticoid receptor (GR).
These data indicate that these substances are able to disrupt the function of the GR as antagonists and metabolism modifies anti-androgenic, anti-glucocorticoid and anti-thyroid hormonal effects of these substances.

Overall, the *in vitro* data indicates possible ED properties, i.e. effect on steroidogenesis, of the substance, relevant for both the environment and human health.

7.10.2.2. *In vivo* data

In vivo data with mixtures containing TBPH is available.
The fire-retardant product FM 550 contains four components: Triphenyl phosphate (TPP), a mixture of isopropylated triphenylphosphate isomers (ITPs), ethylhexyl-tetrabromobenzoate (TBB) and TBPH. A study with, Firemaster 550, was performed to evaluate its possible endocrine disrupting effects (Patisaul *et al*., 2013). Rats were exposed by the oral route to 100 or 1000 µg/day across gestation and lactation.

Data showed disruption of the thyroid hormone system in the dams. The total serum thyroxine (T4) level was dose-dependently elevated in dams with statistical significance at the high dose, whereas there was a decrease in T4 in pups. Serum triiodothyronine (T3) levels in dams were decreased without statistical significance. It is unclear why T4 levels increased. No effects on hepatic deiodinase activity were observed, suggesting the increase in T4 was not due to inhibition of outer ring deiodination. There is no evidence that TBB or TBPH inhibit the activity of conjugating systems responsible for clearing T4 from the body.
In the pups the most distinctive effect was a statistically significant increased body weight of the offspring in the high-dose group compared to the control. This was observed in both sexes starting at PND 10 for males and PND 21 for female pups. This significant overweight was retained into adulthood (PND 220). In female pups, pubertal onset was significantly advanced at the high dose. This effect was associated with elevated body weights. Increased body weight is a contributing factor, but hormonally active compounds may also play a role.
The behavioural testing data suggest sex-specific effects on exploratory and anxiety-related behaviour.

In conclusion, the available *in vivo* data, relevant for the assessment of potential ED properties of TBPH is limited. Information from the study with a mixture, containing TBPH, indicates possible ED properties of the mixture including effect on the thyroid hormone levels and puberty. However, no conclusion can be drawn from this data for the substance, as the observed effects may be caused by the other components of the tested mixture.

7.10.3. Conclusion on endocrine disrupting properties (combined/separate)

There are indications for ED properties of the substance, based on the *in vitro* data. However, these indications cannot be confirmed *in vivo*, based on the available information. However, the substance has been concluded to meet the vPvB-criteria of REACH (see section 7.11). The evaluating Member State did therefore not consider anye information request in order to further assess potential ED properties.

7.11. PBT and vPvB assessment

Persistence

Available hydrolysis data are contradictory. A hydrolysis study sponsored by the registrant reports a DT_{50} of 14.7 days for TBPH in a 1% acetonitrile solution at pH7 and 20°C extrapolated from 50. Contradictory to this a hydrolysis half-life > 1year at pH 4, 7 and 9 is reported by Canadian authorities in their evaluation of TBPH (Environment and Climate Change, Health Canada, 2019). Due to its low solubility and high Koc TBPH will be sorbed to particles and mainly distributed to sediment in the aquatic environment. Therefore, hydrolysis is not considered to be a relevant degradation mechanism for TBPH. AopWin v1.92 predicts that TBPH has an atmospheric half-life of 5.8 hours and it is degraded by sunlight when dissolved in different organic solvents. However, TBPH has a very low vapour pressure and is distributed to the particulate phase of the atmosphere. This is confirmed by air monitoring data, also in the air of remote areas proving the Long-range transport potential of TBPH. Photodegradation in the atmosphere is therefore also not considered to be a relevant removal process for TBPH.

Biowin predictions indicate that TBPH is persistent or very persistent to biodegradation and screening studies with very little degradation demonstrated it being not readily biodegradable. This is confirmed by the results from an enhanced ready test performed according to OECD guideline 302C (7% degradation in 28 days). REACH guidance R11 states "*Lack of degradation (<20% degradation) in an inherent biodegradability test equivalent to the OECD TG 302 series may provide sufficient information to confirm that the P-criteria are fulfilled without the need for further simulation testing for the purpose of PBT/vPvB assessment. Additionally, in specific cases it may be possible to conclude that the vP-criteria are fulfilled with this result if there is additional specific information supporting.*

No simulation study is available but a DT50>200 d is reported from a non-guideline outdoor mesocosm study. This value may not be directly comparable to the vP-criterion of REACH Annex XIII, but it strongly indicates that TBPH is very persistent in sediment. Furthermore, the presence of TBPH in all environmental compartments including air, surface water, sediment, and biota, also in remote areas such as the Arctic, gives further support to conclude that the substance is very recalcitrant to degradation.

Overall, based on the available information the evaluating MSCA considers that TBPH fulfils the vP criterion of REACH.

Bioaccumulation

With a log Kow of 10.5 and a molecular weight of 706 g/mol TBPH is not expected to be readily absorbed. This is confirmed by toxicokinetic studies showing that the major part of a given dose is excreted unchanged. However, a small fraction of the substance is absorbed and accumulates in tissues of the exposed organisms. That TBPH is taken up by biota is confirmed by monitoring data. TBPH has been detected in biota (fish, birds, mammals) including arctic species such as the polar bear. Likewise in the available fish dietary bioaccumulation studies only a small part of the total given doses was found in the fish at the end of the uptake period. This is probably due to that TBPH is poorly absorbed in the gut of the fish and not because of metabolism and excretion. BMFs were measured in two of the studies. The BMFs were low and of similar magnitude in both studies (0.02 for Atlantic killifish, (*Fundulus heteroclitus*) and 0.038 for Rainbow trout (*Oncorhynchus mykiss*) suggesting that TBPH is not vB according to the REACH Annex XIII criterion.

Contrary to this, all 15 models within the OECD TG 305 BCF estimation tool except 1 predicts BCFs> 5000. However, most of the models are based on a predicted uptake rate constant which considering the low uptake seen in the bioaccumulation studies may be

overestimated, thus overestimating the BCF of TBPH. It is also noted that, according to the OECD guidance document on aspects of OECD TG 305 (OECD 2017), the log Kow of TBPH (10.2) is higher than the applicability domain of all these models. Furthermore, the model where a BCF < 2000 was derived was developed from data on Carp (*Cyprinus carpio*) and the applicability for other species is unknown. On the other hand, TBPH is poorly metabolised by fish and the depuration rate is slow. Comparing the non-corrected depuration rate constants from the dietary bioaccumulation studies with the criteria proposed by Brooke and Crookes, 2012 (K_2 of 0.085 equals - BCF 5000 and a K_2 of 0.178 equals BCF 2000) suggests that TBPH is very bioaccumulative, i.e. has a BCF>5000.

Furthermore, a TMF of 2.42 for TBPH has been measured in an aquatic food chain study from China, indicating trophic magnification. In addition, Jin *et al* (2016) found a positive correlation between trophic level and TBPH concentration in resident birds of Korea. Finally, the ubiquitous presence of TBPH in biota (mussel, fish, birds, mammals) also in arctic species such as ringed seal and polar bear gives further indication that TBPH is very bioaccumulating.

The evaluating Member State therefore considers that TBPH fulfils the vB criterion of REACH.

Toxicity

The available toxicity data (environmental as well as mammalian) indicates that TBPH does not fulfil the T-criterion of REACH Annex XIII.

Overall conclusion

The overall conclusion of the PBT-assessment is that TBPH is a vPvB substance according to the criteria of REACH Annex XIII.

7.12. Exposure assessment

7.12.1. Human health

Not assessed.

7.12.2. Environment

7.12.3. Not assessed Combined exposure assessment

Not assessed.

7.13. Risk characterisation

Not performed.

7.14. References

Arinaitwe K *et al* (2014) Polybrominated Diphenyl Ethers and Alternative Flame Retardants in Air and Precipitation Samples from the Northern Lake Victoria Region, East Africa. Environ. Sci. Technol. 48, 1458-1466.

Baldwin K R, Phillips A L, Horman B, Arambula S E, Rebuli M E, Stapleton H M and Patisaul H B (2017) Sex specific accumulation and behavioral effects of developmental Firemaste 550 exposure in Wistar rats. Scientific Reports | 7: 7118 | DOI:10.1038/s41598-017-07216-6

Bearr JS, Stapleton HM, Mitchelmore CL (2010). Accumulation and DNA damage in fathead minnows (Pimephales promelas) exposed to 2 brominated flame-retardant mixtures, Firemaster1 550 and Firemaster1 BZ-54. Environ Toxicol Chem 29, 722–729.

Brookes and Crookes, 2012 Depuration rate constant: growth correction and use as an indicator of bioaccumulation potential. Environment Agency, Horizon House, Deanery Road, Bristol, BS1 5AH

Davis E F and Stapleton H M (2009). Photodegradation Pathways of Nonabrominated Diphenyl Ethers, 2-Ethylhexyltetrabromobenzoate and Di(2-ethylhexyl)tetrabromophthalate: Identifying Potential Markers of Photodegradation. Environ. Sci. Technol 43, 5739-5746.

de Jourdan BP, Hanson ML, Muir DC, *et al*. (2013) Environmental fate of three novel brominated flame retardants in aquatic mesocosms. Environ Toxicol Chem 32(5):1060-1068.

Egloff C, Crump D, Chiu S, Manning G, McLaren K K, Cassone C G, Letcher R J, Gauthier L T, Kennedy S W (2011) In vitro and in ovo effects of four brominated flame retardants on toxicity and hepatic mRNA expression in chicken embryos. Toxicology Letters 207, 25-33.

Environment and Climate Change Canada, Health Canada (2019) State of the Science Report, Certain Organic Flame Retardants Substance TBB and TBPH. Cat. No.: En14-368/2019E-PDF. ISBN 978-0-660-30004-7.

Ezechiaš M, Svobodova K, Cajthaml T (2012) Hormonal activities of new brominated flame retardants, Chemosphere 87, 820–824.

Fernie K J, Chabot D, Champoux L, Brimble S, Alaee M, Marteinson S, Chen D, Palace V, Bird D M, Letcher R J, (2017) Spatiotemporal patterns and relationships among the diet, biochemistry, and exposure to flame retardants in an apex avian predator, the peregrine falcon. Environmental research 158, 43-53.

Ganci Aristide P., Vane Christopher H, Abdallah Mohamed A.-E., Moehring Thomas, Harrad Stuart. Legacy PBDEs and NBFRs in sediments of the tidal River Thames using liquid chromatography coupled to a high-resolution accurate mass Orbitrap mass spectrometer. Science of The Total Environment 658, 1355-1366.

Gentes M, Letcher RJ, Caron-Beaudoin E, *et al*. (2012) Novel flame retardants in urban-feeding ring-billed gulls from the St. Lawrence River, Canada. Environ Sci Technol 46(17):9735–9744.

Guigueno M F, Karouna-Renier N K, Henry P F P, Peters L E, P alace V P, Letcher R J Fernie K J (2018) Sex-Specific Responses in Neuroanatomy of Hatchling American Kestrels in Response to Embryonic Exposure to the Flame Retardants Bis(2-Ethylhexyl)-2,3,4,5-Tetrabromophthalate and 2-Ethylhexyl-2,3,4,5-Tetrabromobenzoate. Environmental Toxicology and Chemistry 9999, 1-9.

Guo J, Romanak K, Westenbroek S, Hites R A, and Venier M (2017) Current-Use Flame Retardants in the Water of Lake Michigan Tributaries. Environ. Sci. Technol. 2017, 51, 9960−9969.

He S *et al*. (2013) Concentrations and trends of halogenated flame retardants in the pooled serum of residents of Laizhou Bay, China. Environmental Toxicology and Chemistry 32, 1242–1247.

Inoue Y, Hashizume N, Yoshida T, Murakami H, Suzuki Y, Koga Y, Takeshige R, Kikushima E, Yakata N and Otsuka M (2012) Comparison of bioconcentration and biomagnification factors for poorly water-soluble chemicals using common carp (*Cyprinus carpio L.*). Archive of Environmental Contamination and Toxicology, 63(2), 241-248.

Jin X, Lee S, Jeong Y, Yu J P, Kee Baek W´, Shin K H, Kannan K, Moon H B (2016) Species-specific accumulation of polybrominated diphenyl ethers (PBDEs) and other emerging flame retardants in several species of birds from Korea. Environmental Pollution 219 (2016) 191-200.

KLIF (2013) Perfluorinated alkylated substances, brominated flame retardants and chlorinated paraffins in the Norwegian Environment - Screening 2013. Report M 40 Miljødirektoratet, Norway.

KLIF (2014) Environmental Contaminants in an Urban Fjord. Report M 2015 MiljØdirektoratet, Norway.

Klopcic I *et al*. (2016) Comparison of in vitro hormone activities of novel flame retardants TBB, TBPH and their metabolites TBBA and TBMEPH using reporter gene assays. Chemosphere 160, 244-251.

Klosterhaus S L, Stapleton H M, La Guardia M J, Greig DJ (2012) Brominated and chlorinated flame retardants in San Francisco Bay sediments and wildlife. Environment International 47 (2012) 56–65.

Knudsen GA *et al*. (2017) Disposition of the emerging brominated flame retardant, bis(2-ethylhexyl) tetrabromophthalate, in female Sprague Dawley rats: effects of dose, route and repeated administration. Xenobiotica 47, 245-254.

La Guardia MJ, Hale RC, Harvey E, *et al*. (2012) In situ accumulation of HBCD, PBDEs, and several alternative flame-retardants in the bivalve (*Corbicula fluminea)* and gastropod (*Elimia proxima*). Environ Sci Technol 46(11):5798-5805.

La Guardia MJ, Hale RC and Newman B (2013). Brominated Flame-Retardants in Sub-Saharan Africa: Burdens in Inland and Coastal Sediments in the eThekwini Metropolitan Municipality, South Africa. Environ Sci Technol 47, 9643-9650.

Lam JC, Lau RK, Murphy MB, *et al*. (2009) Temporal trends of hexabromocyclododecanes (HBCDs) and polybrominated diphenyl ethers (PBDEs) and detection of two novel flame retardants in marine mammals from Hong Kong, South China. Environ Sci Technol 43(18):6944-6949.

Lazarus R S, Rattner B A, McGowan P C, Hale R C, Karouna-Renier N K, Erickson R A and Ottinger M A (2016) Chesapeake bay Fish-osprey (*Pandion Haliaetus*) food chain: Evaluation of contaminant exposure and genetic damage. Environmental Toxicology and Chemistry 35, 1560-1575.

Li *et al* (2016) Five-year trends of selected halogenated flame retardants in the atmosphere of Northeast China. Science of the total environment 539, 286-293.

Liu L Y, Salamova A, Venier M, Hites RA (2016) Trends in the levels of halogenated flame retardants in the Great Lakes atmosphere over the period 2005–2013. Environment International 92–93 (2016) 442–449.

Ma, Y.; Venier, M.; Hites, R. A. (2012) 2-Ethylhexyltetrabromobenzoate and Bis(2-ethylhexyl) Tetrabromophthalate Flame Retardants in the Great Lakes Atmosphere. Environ. Sci. Technol. 2012, 46 (1), 204−208.

Mankidy R, Ranjan B, Honaramooz A, Giesy JP (2014) Effects of novel brominated flame retardants on steroidogenesis in primary porcine testicular cells, Toxicology Letters 224, 141-146.

McGee S P, Konstatinov A, Stapleton H M, Volz D C (2013) Aryl phosphate esters within a major PentaBDE replacement product induce cardiotoxicity in developing Zebrafish embryos: Potential role of the aryl hydrocarbon receptor. Toxicological sciences 133(1), 144–156.

Möller A, Xie Z, Sturm R and Ebinghaus R (2011a) Polybrominated diphenyl ethers (PBDEs) and alternative brominated flame retardants in air and seawater of the European Arctic. Environmental Pollution 159, 1577-1583.

Möller A, *et al*. (2011b) Polybrominated diphenyl ethers vs alternate brominated flame retardants and dechloranes from East Asia to the Arctic. Environ Sci Technol 45, 6793-6799.

Möller A, *et al*. (2012) Brominated flame retardants and dechlorane plus in the marine atmosphere from Southeast Asia toward Antarctica. Environ Sci Technol 46:3141-3148.

Nacci D, Clark,B, Guardia MJ, Miller K, Champlin D, Kirby I, Bertrand A and Jayaramana S (2018) Bioaccumulation and Effects of Dietary Exposure to the Alternative Flame Retardant, Bis(2-Ethylhexyl) Tetrabromophthalate (TBPH), in the Atlantic Killifish, Fundulus heteroclitus. Environ Toxicol Chem 37(9): 2350-2360.

OECD (2017) Guidance Document on Aspects of OECD TG 305 on Fish Bioaccumulation. Series on Testing & Assessment No. 264. ENV/JM/MONO (2017)16.

Olunkunle, O I, Okonkwo, O J (2015) Concentrations of novel brominated flame retardants and HBCD in leachates and sediments from selected municipal solid waste landfill sites in Gauteng Province, South Africa, Waste Manage., 43, 300-421.

Patisaul HB, Roberts SC, Mabrey N, McCaffrey KA, Gear RB, Braun J, Belcher SM, Stapleton HM (2013) Accumulation and endocrine disrupting effects of the flame retardant mixture Firemaster® 550 in rats: an exploratory study, J Biochem Molecular Toxicology 27, 124-136.

Roberts SC, Macaulay LJ, Stapleton HM (2012) In vitro metabolism of the brominated flame retardants 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) and bis(2-ethylhexyl) 2,3,4,5-tetrabromophathalate (TBPH) in human and rat tissues, Chem Res Toxicol 16, 25(7):1435-1441.

Sagerup K, Herzke D, Harju M, *et al*. (2010) New brominated flame retardants in Arctic biota. Statlig program for forurensningsovervåking. http://www.klif.no/publikasjoner/2630/ta2630.pdf.

Salamova A, Hermanson M and Hites R (2014) Organophosphate and Halogenated Flame Retardants in Atmospheric Particles from a European Arctic Site. Environmental Science & Technology 48, 6133-6140.

Saunders DMV, Higley EB, Hecker M, Mankidy R, Giesy JP (2013) In vitro endocrine disruption and TCDD-like effects of three novel brominated flame retardants: TBPH, TBB, & TBCO, Toxicology Letters 223, 252– 259.

Saunders DMV, Podaima M, Codling G, Giesy JP, Wiseman S (2015) A mixture of the novel brominated flame retardants TBPH and TBB affects fecundity and transcript profiles of the HPGL-axis in Japanese medaka. Aquatic Toxicology 158, 14-21.

Schlabach M, *et al* (2011) Brominated Flame Retardants (BFR) in the Nordic Environment. Tema Nord 2011:528.

Shoeib M, Ahrens L, Jantunen L and Harner T (2014) Concentrations in air of organobromine, organochlorine and organophosphate flame retardants in Toronto, Canada, Atmospheric Environment 99, 140-147.

Silva MJ, Hilton D, Furr J, Gray LE, Preau JL, Calafat AM, Ye X (2015) Quantification of tetrabromo benzoic acid and tetrabromo phthalic acid in rats exposed to the flame retardant Uniplex FRP-45, Arch Toxicol 90, 551-557.

Unpublished (2018) Dietary bioaccumulation in O. mykiss.

USEPA (2015) TSCA Work Plan Chemical Problem Formulation and Data Needs Assessment Brominated Phthalates Cluster Flame Retardants. EPA Document# 740-Q1-4004.

Venier M, Dove A, Romanak K, Backus S, Hites R (2014) Flame retardants and legacy chemicals in Great lakes' water. Environ Sci Technol 48, 9563-9572.

Vorkamp K, Bossi R, Ríget F, Skov H, Sonne C, Dietz R (2015) Novel brominated flame retardants and dechlorane plus in Greenland air and biota. Environmental Pollution 196, 284-291.

Wedebye, Nikolov, Nielsen, Boberg, Axelstad, Klein, Reffstrup and Dybdahl. (2016). Category approach for selected brominated flame retardants: The Danish Environmental Protection Agency ISBN no. 978-87-93435-90-2
https://www2.mst.dk/Udgiv/publications/2016/07/978-87-93435-90-2.pdf.

Xiao H, Shen L, Su Y, *et al*. (2012) Atmospheric concentrations of halogenated flame retardants at two remote locations: the Canadian High Arctic and the Tibetan Plateau. Environ Pollut 161, 154-161.

Yu Y, Hung H, Alexandrou N, Roach P, Nordin K (2015) Multiyear measurements of flame retardants and organochlorine pesticides in air in Canada's western sub-arctic. Environ Sci Technol 49, 8623-8630.

Zheng G, Wan Y, Shi S, Zhao H, Gao S, Zhang S, An L, Zhan Z. (2018).Trophodynamics of emerging brominated flame retardants in the aquatic food web of Lake Taihu: Relationship with organism metabolism across trophic levels. Environ Sci Technol 52, 4632–4640.

Zhu B, Lam J.C.W., Yang S, Lam P.K.S. (2013). Conventional and emerging halogenated flame retardants (HFRs) in sediment of Yangtze River Delta (YRD) region, East China. Chemosphere 93, 555-560.

Zhu B, Lai N, Wai T C, Chan L L, Lam J C Lam P K (2014) Changes of accumulation profiles from PBDEs to brominated and chlorinated alternatives in marine mammals from the South China Sea. Environment International 66 (2014) 65–70.

Zhou SN *et al*. (2014) Measurements of Selected Brominated Flame Retardants in Nursing Woman: Implications for Human Exposure. Environ. Sci. Technol. 48, 8873-8880.

7.15. Abbreviations

BFR Brominated Flame Retardant
CBI Confidential Business Information
CDR Chemical Data Reporting
CPSC Consumer Product Safety Commission
DEHP bis (2-ethylhexyl) phthalate
DNA Data Needs Assessment
EC European Commission
ECHA European Chemicals Agency
ED Endocrine Disruptor
EPA Environmental Protection Agency
FR Flame Retardant
HPV High Production Volume
KOW Octanol:Water partition coefficient
LOEL Lowest Observed Effect Level
Log KOW: Logarithmic octanol:water partition coefficient
NICNAS National Industrial Chemicals Notification and Assessment Scheme
NOAEL No-observed-adverse-effect level
OCSPP Office of Chemical Safety and Pollution Prevention
OECD Organisation for Economic Co-operation and Development
OPPT Office of Pollution Prevention and Toxics
OSHA Occupational Safety and Health Administration
PBDE Polybrominated Diphenyl Ether
PentaBDE Pentabrominated diphenyl ether
PFA Polyurethane Foam Association
PUF Polyurethane foams
PVC Polyvinylchloride
QSAR Quantitative Structure-Activity Relationship
SVOCs Semi-volatile organic chemicals
TBB Benzoic acid, 2, 3, 4, 5-tetrabromo-, 2-ethylhexyl ester
TBPH 1, 2-Benzenedicarboxylic acid, 3, 4, 5, 6-tetrabromo-, 1, 2-bis (2-ethylhexyl) ester
TBPA-Diol Generic designator that is used for 1, 2-Benzenedicarboxylic acid, 3, 4, 5, 6-tetrabromo-, 1-[2-(2-hydroxyethoxy) ethyl] 2-(2-hydroxypropyl) ester