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Novel brominated flame retardants - A review of their occurrence in indoor air, dust, consumer goods and food

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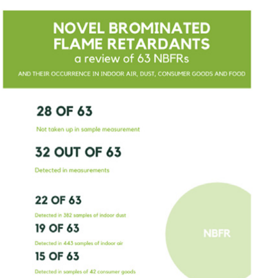
GRAPHICAL ABSTRACT



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ABSTRACT

This critical review summarizes the occurrence of 63 novel brominated flame retardants (NBFRs) in indoor air, dust, consumer goods and food. It includes their EU registration and (potential) risks. The increasing application of NBFRs calls for more research on their occurrence, environmental fate and toxicity. This review reports which NBFRs are actually being studied, which are detected and which are of most concern. It also connects data from the European Chemical Association on NBFRs with other scientific information. Large knowledge gaps emerged for 28 (out of 63) NBFRs, which were not included in any monitoring programs or other studies. This also indicates the need for optimized analytical methods including all NBFRs. Further research on indoor environments, emission sources and potential leaching is also necessary. High concentrations of 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (EH-TBB), bis(2-ethylhexyl)tetrabromophthalate (BEH-TEBP), decabromodiphenyl ethane (DBDPE) and 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE) were often reported. The detection of hexabromobenzene (HBB), pentabromotoluene (PBT), 1,4-dimethyltetrabromobenzene (TBX), 4-(1,2-dibromoethyl)-1,2-dibromocyclohexane (DBE-DBCH) and tetrabromobisphenol A bis(2,3-dibromopropyl) ether (TBBPA-BDBPE) also raises concern.

1. Introduction

Flame retardants (FRs) are a large group of chemicals used in different materials to delay or prevent flaming. Many are based on bromine, chlorine or phosphorus, or a mix of these, but others such as metal-based FRs and melamine also occur. They prevent flaming

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by quenching and cooling (metal-based FRs), by formation of solid phase char (melamine-based and phosphorus-based FRs), form a stable foam layer that acts as a barrier between the flames and the combustible material (intumescent FRs) (Hörold, 2014), or inhibition by radical formation in the vapor phase, for which brominated FR (BFRs) are commonly used (Laoutid et al., 2009). The production and application of BFRs have dramatically increased in the past thirty years (Liagkouridis et al., 2015). Most BFRs have toxic properties and a negative impact (persistence, bioaccumulation) on the environment. Polybrominated biphenyls (PBBs) were already restricted in 1984 (Directive 83/264/EEC) and their production ceased in 2000 (Kemmlein et al., 2009). The United Nations Stockholm Convention listed penta-brominated diphenylethers (BDEs) and octa-BDE as Persistent Organic Pollutants (POP) in 2009 (Stockholm Convention). In 2017, the deca-BDE was added to the POP list under the Stockholm Convention. Hexabromocyclododecane (HBCD or HBCDD) was added to the POP list in 2013 and has been phased out in many fields by 2016, except in China (Shi et al., 2018). Since the ban on PBDEs and HBCDD novel BFRs (NBFRs) have emerged (Bergman et al., 2012). NBFRs are emerging contaminants which are present in materials and can reach the environment, and which are relatively new on the market (Covaci et al., 2011). These "novel", "emerging" or "new" BFRs have many different properties due to their varying physico-chemical properties and are, therefore, applied in a wide range of products, such as plastics, foams, textiles, furniture and electronic devices (Covaci et al., 2011; Shi et al., 2018). Studies suggest health and environmental risks potentially related to the exposure of NBFRs (Li et al., 2019). The European Food Safety Authority (EFSA) published a scientific report on emerging and novel brominated flame retardants in food, but could not perform risk assessments due to limited data on occurrence and toxicity (EFSA, 2012). Currently there are recommendations by the European Commission (Directive, 2014/118/EU) on monitoring traces of BFRs in food, of which a few NBFRs (such as 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (EH-TBB)).

NBFRs can leach into the indoor environment because most of them are not covalently linked to the polymers to which they are added. Consequently, the presence of NBFRs in materials and consumer goods in homes and public spaces leads to exposure to humans. To our current understanding of BFRs, there are four main ingestion routes for human exposure: ingestion via indoor dust, inhalation via indoor air, uptake via our diet and uptake through the skin. It is reasonable to propose similar routes for NBFRs (Covaci et al., 2011), as most BFRs are lipophilic. The resemblance of NBFRs and legacy BFRs makes it likely that many NBFRs are also toxic and bioaccumulative and have adverse effects on human health and environment. Different reports have already suggested this (Ali et al., 2011; Gramatica et al., 2016; McGrath et al., 2018). Gramatica et al. (2016) showed that emerging BFRs are not necessarily safer and often more hazardous than restricted BFRs. The substitution of legacy BFRs by NBFRs is therefore often called 'regrettable substitution'.

Information on NBFR production volumes, use and occurrence is still limited, which makes it difficult to assess potential environmental and health risks (Iqbal et al., 2017). In 2009, the total production of NBFRs was estimated between 100 000 and 180 000 tonnes per year (Papachlimitzou et al., 2012). Current production volumes are hard to find. Due to phasing out legacy BFRs, it is likely this volume has increased. Several organophosphorus FRs have been introduced as substitutes for some of the legacy BFRs. Firemaster 550 and Firemaster BZ-54, containing 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (EH-TBB) and/or bis(2-ethylhexyl)tetrabromophthalate (BEH-TEBP), were introduced as alternatives for pentaDBE (Tao et al., 2016). When decaBDE was banned, decabrominated diphenylethane (DBDPE) was introduced as an alternative (McGrath et al., 2018). Tetrabromobisphenol A (TBBPA)[1] was approved by the EU in 2008, after an eight-year risk assessment. Since then, its production and application has increased hugely. It has been put forward as an alternative for pentaDBE (ECHA, 2019).

In most countries there are no laws to monitor the use of NBFRs (Pereira et al., 2015). Production of NBFRs in the United States (US) is registered and reported by Chemical Data Reporting (CDA), part of the US Environmental Protection Agency (US EPA). However, their data on production volumes of NBFRs are often non-existent or "confidential business information" (CBI) (EPA , 2016). The European Chemicals Agency (ECHA) registers and monitors data on chemicals used in the European Union (it implements REACH[2]) (ECHA, 2019) and EFSA recommended monitoring (novel)BFRs in feed and food (EFSA, 2012). Most NBFRs are produced (and used) in China. No central data reporting agency can be accessed in China to provide numbers on production (Li et al., 2019). This would be crucial to make a current general estimation on NBFR production volumes. The 100 000–200 000 tonnes/yr producton volumes mentioned by Papachlimitzou et al. (2012) for 2009 emphasize, however, that more recent global production information is badly needed. The total production volume of polychlorinated biphenyls (PCBs) ever was ca. 1.3 million tonnes. If the 100 000–180 000 tonnes have continued or even grown since 2009, the 1.3 million tonnes would have been exceeded meanwhile.

In the past ten years, detailed reviews on NBFRs have been sparse. There are critical reviews on NBFRs in soil and sediments (McGrath et al., 2017; Jans, 2016), in the Arctic (de Wit et al., 2010), on their ecotoxicity and biodegradability (Ezechiáš et al., 2014) and on methodologies used for analysis (Papachlimitzou et al., 2012). Covaci et al. (2011) published a detailed review on thirteen NBFRs to summarize their production, environmental fate and occurrence. They give a summary of current literature on extraction and analysis of NBFRs in sea and freshwater, sewage sludge, sediment and soil and air as well as in biota. Human exposure to NBFRs was also discussed. Their review highlights certain research gaps in analytical methodology, environmental and human exposure (Covaci et al., 2011). Lucattini et al. (2018) published a review on semi-volatile compounds (SVOCs) in indoor dust, air and consumer goods, which included a number of NBFRs. However, (N)BFRs were only a small part of the whole review (Lucattini et al., 2018). There is certainly still a knowledge gap when it comes to which NBFRs are being used and on their levels in goods, dust, indoor air and food.

This review is an attempt to shed some light on these topics. We collected recent information on 63 NBFRs, their occurrence in the indoor environment and in food. Until now such literature research, summarizing so many NBFRs, was not carried out yet. The goal of this research was to review current literature on NBFRs as regards their registration at the European Chemicals Agency (ECHA), their occurrence in the indoor dust, indoor air, consumer goods and in food. Literature was systematically analyzed. It concludes with knowledge gaps that were identified.

2. Search criteria

In total, information on 63 different NBFRs was identified. If available, abbreviations from Bergman et al. (2012) were used.

[1] TBBPA is not a legacy BFR, as it is not restricted. However, it also not really a novel BFR. It is globally the most commonly used BFR (Sun et al., 2019).

[2] REACH: **R**egistration, **E**valuation, **A**uthorization and restriction of **Ch**emicals. REACH includes legislation on chemicals: it includes procedures on registration of chemicals and evaluation of chemical properties and (potential) risks (ECHA, 2019).

Different isomers/congeners were counted as one NBFR. The Web of Science database was used (April & May 2019), without specifying geographical area but setting a limit for studies based on their publishing year. A general search was conducted using the keywords [novel brominated flame retardant], [emerging brominated flame retardant] and [new brominated flame retardant] with a time limit set to 2015–2019. A total of 177 articles were selected for evaluation. Another search for each of the 63 NBFRs was performed using specifically each NBFR name, abbreviations from Bergman et al. (2012) and trade names. The time limit was set to ten years: 2009–2019.[3] Another 111 articles resulted from this search of which a total of 83 articles were selected. Nevertheless, for 19 NBFRs no suitable literature was found (indicated in Fig. 1). For nine NBFRs very little literature (only one or two articles) was found. The authors have chosen for occurrence in the indoor environment and therefore including (indoor) air, dust, goods and food. They acknowledge this might be an arbitrary choice, excluding important areas such as outdoor air or soil. However, limitation of the research scope is necessary. Furthermore, a very detailed review on environmental occurrence of NBFRs in sea and freshwater, sewage sludge, sediment and soil and air as well as in biota, was written by Covaci et al. (2011).

3. Overview NBFRs

Table 1 gives an overview of the 63 NBFRs studied. It includes database information from the European Chemicals Agency (ECHA). It also contains summarized information from the European REACH program, including suspected toxicity or persistence. Volumes and other information on use and production are included if these were available.

Table 1 shows that the REACH program is well aware of the existence of most NBFRs. There is information on hazardous effects, toxicity and bio accumulatively and/or PBT/vPvB assessment on 51 NBFRs. However, in 12 cases, no information of effects and behavior is available in the REACH database: for PBBC, TBPD-TBP, TBBPS-BME, TBBPA-BA, TBBPA-BP, OBTMPI, DBDBE, DBP-TAZTO, BDBP-TAZTO, BATE, tetrabromobenzoic acid, and tetraBRP. The datasheets of ECHA do not always include CAS-nos., making it difficult to search, especially because for some NBFRs different names exist. If no information is found, it may also mean no company is either producing or using the substance. However, more worrying is that in only 13 cases there is information available on the production volumes: 2 times 1–10 tonnes per year, 3 times 10–100tonnes/yr, 5 times 100–1000 tonnes/yr, 2 times 1000–10,000 tonnes/yr (TBBPA-BDBPE and TTBP-TAZ), and one time 10 000–100,000 tonnes/yr (DBDPE). So, for fifty compounds no information on production within the European economic area is available. At the same time, many of these fifty NBFRs are suspected carcinogen, suspected hazardous to the environment, suspected mutagen, suspected skin irritant, suspected skin sensitiser, suspected respiratory sensitiser, suspected toxic for reproduction, suspected toxic via the oral route, suspected bioaccumulative or suspected persistent in the environment. Thirty-three out of the 40 NBFR for which information is available in REACH are suspected persistent in the environment. Although 'suspected' means that more proof would be needed to arrive at such a conclusion, this table adds to the expectation that many of the NBFRs, in line with the traditional BFRs such as PBDEs and HBCDD are persistent. Fourteen NBFRs from this list are suspected bioaccumulative. This information strongly suggests that substitution of halogens very soon leads to PBT compounds (De Boer and Stapleton, 2019). This information shows a huge data gap in production information and in information on effects and behavior of these NBFR.

NBFR concentrations found in the indoor environment vary greatly. The results will be discussed per compound class. To indicate which NBFRs were studied, an overview of standards of NBFRs included in sample measurements is given in Fig. 1. This does not mean that these NBFRs are actually found in the samples. It tells us that many NBFRs were not tested at all and, consequently, there is no information available on their occurrence in materials or the indoor environment. BTBPE, DBDPE and BEH-TEBP were most often included in measurements. These NBFRs are also most often used as replacement of restricted BFRs and, therefore, important to study.

3.1. NBFRs in consumer goods

Literature on NBFRs specifically focusing on consumer goods is limited. The analysis of the various NBFRs in materials is not so easy. Screening for bromine content in goods by XRF is a possible approach. It is an easy and quick method, but an important limitation is that it measures only near surface (5–10 mm) and cannot detect bromine present deeper in the product (Allen et al., 2008). On top of that, XRF can detect bromine in products from other sources than (N)BFRs (Furl et al., 2012), in that way causing false positive results. In part 4.2 literature on indoor dust is discussed, which is indirectly linked to consumer goods as dust from different surfaces and goods is often included in measurements. A distinction between papers was made when data was specifically reported per item (included in this section) or otherwise (next section on indoor dust). Goods and electronics present in homes as well as in public space, e.g. stores and offices, were investigated. From 2009 to 2019, only seven relevant studies were found and evaluated (Ballesteros-Gómez et al., 2014Ballesteros-Gómez et al., 2014; Gallistl et al., 2017; La Guardia and Hale, 2015; Miyake et al., 2017; Nkabinde et al., 2018; Sun et al., 2018; Wu et al., 2018). Table 2 shows collected data on NBFRs: medians of measured items, location and corresponding literature. More data and studies are urgently needed to enable showing of spatial and temporal trends.

Nkabinde et al. (2018) investigated BFRs in consumer goods from South Africa in two steps: first a screening with XRF was carried out to measure bromine in equipment and/or furniture. Secondly, dust samples taken from surfaces of electronics and furniture were analyzed using GC-MS. Concentrations of EH-TBB, BEH-TEBP and BTBPE were reported in many different goods, such as chairs, motherboards and keyboards. Medians varied per product and per NBFR from 14 to 1066 μg/g. In 19 of the 21 consumer good samples, both legacy and novel BFRs were detected. The levels were comparable with results from China and Europe. Sun et al. (2018) analyzed surface dust from different electronics and furniture from China, such as circuit boards, computer casting and sound insulation. They also found HBB, BEH-TEBP and BTBPE. In a study from Germany, many different NBFRs in were detected in dishcloths used for 14 days in a kitchen environment: DBDPE, BATE, TBP-DBPE, ATE, TBP and PBT (Gallistl et al., 2017).

In a study from Wu et al. (2018) foam from different car seats purchased from China, USA and Canada were analyzed and appeared to contain 15 different NBFRs, with high concentrations of DBDPE, which is used as a main substitute of deca-BDE (Wu et al., 2018). A study from the USA showed severe amounts of EH-TBB (mean: 9541 μg/g) and BEH-TEBP (mean: 3578 μg/g) in foam pit. These NBFRs are nowadays added to foam, replacing legacy BFRs (La Guardia and Hale, 2015).

A study in various consumer goods such as televisions and adapters from the Netherlands indicated the presence of 2,4,6-tris(2,4,6-tribromophenoxy)-1,3,5-triazine (TTBP-TAZ)

[3] A larger time limit was chosen due to a limited amount articles.

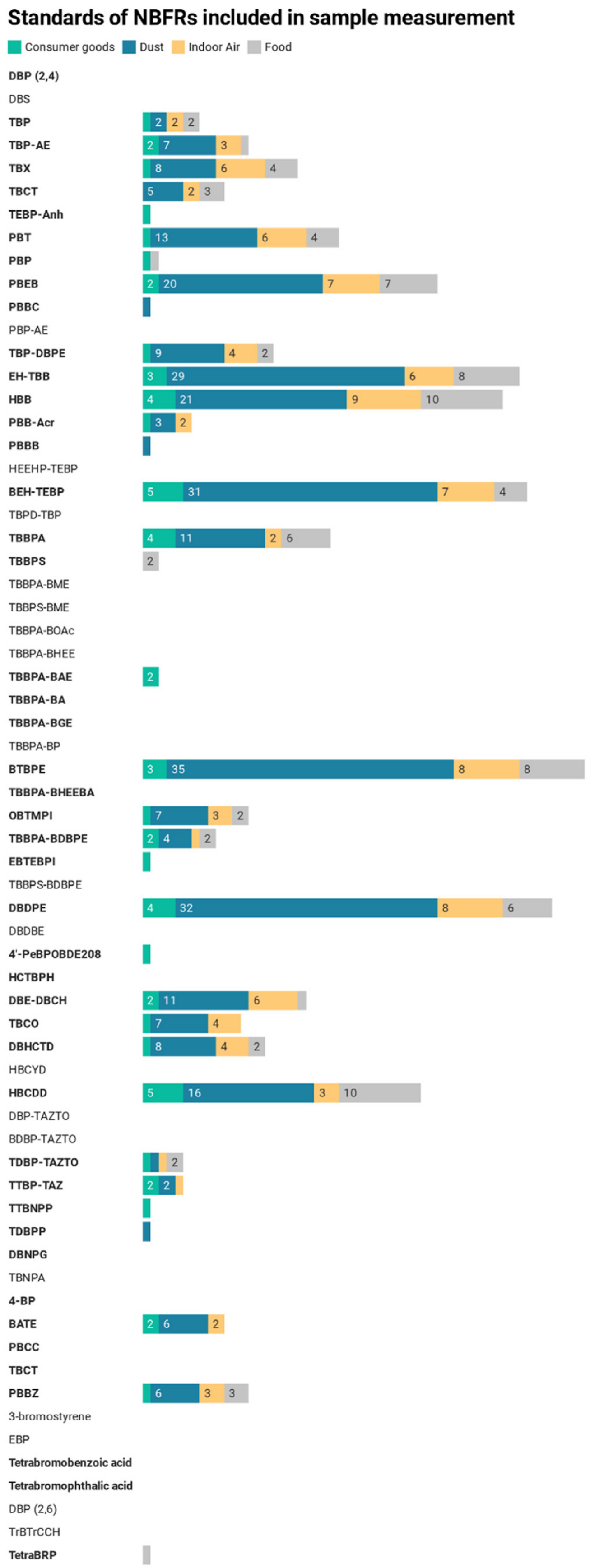

Fig. 1. Overview of NBFR standards included in measurements. The non-bold NBFRs mean no suitable literature was found on these compounds. *HBCDD (legacy BFR) and TBBPA are included in this overview because they were often screened for and detected. Those two are not a NBFR.

(Ballesteros-Gómez et al., 2014Ballesteros-Gómez et al., 2014). It was the only study reporting the presence of TTBP-TAZ, except for one study in Canada in dust and air from e-waste facilities, indicating a very high median in dust of 5540 ng/g (Guo et al., 2018). TTBP-TAZ is a substitute for octaBDE in the polymer Acrylonitrile Butadiene Styrene (ABS), for DecaBDE and hexabromocyclododecane (HBCDD) in high impact polystyrene (HIPS).

3.2. NBFRs in indoor dust

NBFR contamination in indoor dust is a topic in many studies. Dust from many different countries has been studied and various sampling methods have been applied. In the reviewed articles altogether 2555 samples of dust were analyzed. Twenty-five NBFRs were found to be present in indoor dust from various (micro) indoor environments. Fig. 2 shows a map indicating location of the samples and sample size. Europe and China are well represented in the literature, while data from Africa, Australia and South-America is largely missing. Fig. 3 gives an overview of median concentrations of detected NBFRs in indoor dust.

3.2.1. EH-TBB & BEH-TEBP

EH-TBB and BEH-TEBP are often reported in sample measurement of indoor dust, also in high concentrations (up to 1600 ng/g) (Bu et al., 2019; Venier et al., 2016). These two FRs generally serve as major replacement of Penta-BDE and BDE 209, respectively. Consumption of these legacy BFRs is nonetheless still high. No specific data on the production and use of these NBFRs is available, but substantial production is likely (Abbasi et al., 2016; McGrath et al., 2018). A large study in Melbourne, Australia, reported high concentration of EH-TBB (110 ng/g in vehicles). EH-TBB appears to be applied in car interiors and components, in similar concentrations to Penta-BDE mixtures. This study urgently warrants toxicological studies and research on environmental & health effects of NBFRs (McGrath et al., 2018).

Qi et al. (2014) collected indoor dust samples in China and 22 NBFRs were detected with BEH-TEBP being the second dominant FR. A study from Bu et al. (2019) shows the same result: the second dominant NBFR was BEH-TEBP (for both studies the dominant NBFR was DBDPE, see section 4.2.2). Various studies show median concentrations of BEH-TEBP of 15–550 ng/g in dust (Cequier et al., 2014; Cristale et al., 2016; Fromme et al., 2014; Sun et al., 2018; Tang et al., 2019; Tao et al., 2016; Venier et al., 2016) but also higher median concentrations of 550–1300 ng/g have been reported (Bu et al., 2019; Cristale et al., 2016; Sahlström et al., 2015; Peng et al., 2015; Venier et al., 2016).

Various studies show median concentrations of EH-TBB of 100–520 ng/g in dust from homes and workplaces (Dodson et al., 2012; La Guardia and Hale, 2015; Venier et al., 2016; McGrath et al., 2018; Cristale et al., 2016; Sun et al., 2018), but also lower median concentrations were found varying between 0.8 and 20 ng/g (Cequier et al., 2014; Al-Omran and Harrad, 2016; Hassan and Shoeib, 2015; Kuang et al., 2016; Sun et al., 2018; Niu et al., 2019).

3.2.2. DBDPE

DBDPE is often reported in sample measurements in indoor dust, even a median concentration of 4600 ng/g was reported (Tang et al., 2019; Venier et al., 2016). This FR generally serves as major replacement of Deca-BDE. It is especially used in materials used in homes and workplaces (McGrath et al., 2018). A study on indoor dust samples in China detected 22 NBFRs with DBDPE being the dominant FR (Qi et al., 2014). In a large study in twelve countries, much higher concentrations of legacy BFRs were found than of NBFRs, except for DBDPE (Sahlström et al., 2015). DBDPE exceeded

Table 1
Overview of NBFR information including CAS-no., practical abbreviation of NBFR in bold (and if common the previously used abbreviation in classical font) (Bergman et al., 2012), name (according to ECHA), REACH including ECHA annex inventory III[a], PBT/vPvB assessment[b] and use or production (EU) as is given in ECHA, meaning ‘manufactured and/or imported in the European Economic Area’ (ECHA, 2019).

	CAS-no.	NBFR practical abbreviation	Name	REACH	PBT/vPvB assessment [b]	Use or Production
				ECHA Annex Inventory III [a]		
1	615-58-7	**DBP** (24DBP)	2,4-Dibromophenol	Suspected hazardous to the aquatic environment Suspected mutagen Suspected persistent in the environment	No	-
2	31 780-26-4	**DBS**	Dibromostyrene	Suspected hazardous to the aquatic environment Suspected persistent in the environment	No	-
3	118-79-6	**TBP**	2,4,6-Tribromophenol	Very toxic to aquatic life Very toxic to aquatic life with long lasting effects Causes serious eye irritation Harmful if swallowed May cause an allergic skin reaction.	Suspected PBT/vPvB: under assessment, decision postponed.	**10–100 tonnes per year.** Used at industrial sites.
4	3278-89-5	**TBP-AE** (ATE)	2-(Allyloxy)-1,3,5-tribromobenzene	Suspected bioaccumulative Suspected persistent in the environment:	No	–
5	23 488-38-2	**TBX**	2,3,5,6-Tetrabromo-p-xylene	Suspected bioaccumulative Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser Suspected toxic for reproduction	No	–
6	39 569-21-6	**TBCT**	2,3,4,5-Tetrabromo-6-chlorotoluene	Suspected bioaccumulative Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser	No	–
7	632-79-1	**TEBP-Anh** (TBPA)	Tetrabromophthalic anhydride	May cause an allergic skin reaction.	No	**10–100 tonnes per year.** Used in polymers and produced to use in chemicals and plastic products.
8	87-83-2	**PBT**	2,3,4,5,6-Pentabromotoluene	Suspected bioaccumulative Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser	No	–
9	608-71-9	**PBP**	Pentabromophenol	Suspected hazardous to the aquatic environment Suspected persistent in the environment	No	–
10	85-22-3	**PBEB**	2,3,4,5,6-Pentabromoethylbenzene	Suspected bioaccumulative Suspected persistent in the environment	No	–
11	58 495-09-3	**PBBC**	Pentabromobenzyl chloride	No results were found	No results were found	–
12	3555-11-1	**PBP-AE** (PBPAE)	Allyl pentabromophenyl ether	May cause long lasting harmful effects to aquatic life.	No	–
13	35 109-60-5	**TBP-DBPE** (DPTE)	1,3,5-Tribromo-2-(2,3-dibromopropoxy) benzene	Suspected bioaccumulative Suspected carcinogen	No	–

(*continued on next page*)

Table 1 (*continued*)

	CAS-no.	NBFR practical abbreviation	Name	REACH ECHA Annex Inventory III [a]	PBT/vPvB assessment [b]	Use or Production
				Suspected persistent in the environment		
14	183 658-27-7	**EH-TBB** (EHTBB)	2-Ethylhexyl 2,3,4,5-tetrabromobenzoate	As reaction mass for BEH-TEBP: Very toxic to aquatic life Very toxic to aquatic life with long lasting effects May cause an allergic skin reaction	–	Data production confidential
15	87-82-1	**HBB**	Hexabromobenzene	Suspected bioaccumulative Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser	No	–
16	59 447-55-1	**PBB-Acr**	(Pentabromophenyl)methyl acrylate	Causes serious eye irritation May cause an allergic skin reaction	No	**100–1000 tonnes per year.** ECHA has no public registered data.
17	38 521-51-6	**PBBB**	2,3,4,5,6,α-Hexabromotoluene	Suspected carcinogen Suspected persistent in the environment Suspected skin sensitiser	No	–
18	20 566-35-2	**HEEHP-TEBP**	2-(2-Hydroxyethoxy)ethyl 2-hydroxypropyl 3,4,5,6-tetrabromophthalate	This substance has not been registered under the REACH Regulation No hazards have been classified.		Manufactured to use in plastic products and used as intermediate.
19	26 040-51-7	**BEH-TEBP** (BEHTEBP, TBPH)	Bis(2-ethylhexyl) tetrabromophthalate	Very toxic to aquatic life Very toxic to aquatic life with long lasting effects May cause an allergic skin reaction	Potential PBT or vPvB substances: decision deferred.	**100–1000 tonnes per year and tonnage confidential** Produced to use in plastic and rubber products.
20	168 434-45-5	**TBPD-TBP** (TBPTP)	3-(Tetrabromopentadecyl)-2,4,6-tribromophenol	No results were found	No results were found	–
21	39 635-79-5	**TBBPS** (TBBP-S)	4,4′-Sulphonylbis [2,6-dibromophenol]	Suspected mutagen Suspected persistent in the environment Suspected toxic for reproduction	No	–
22	37 853-61-5	**TBBPA-BME** (TBBPA ME)	4,4’-(Isopropylidene)bis [2,6-dibromoanisole]	Suspected bioaccumulative Suspected hazardous to the aquatic environment Suspected persistent in the environment	No	–
23	70 156-79-5	**TBBPS-BME**	Tetrabromobisphenol S bismethyl ether	No results were found	No results were found	–
24	33 798-02-6	**TBBPA-BOAc**	4,4′-Isopropylidenebis [2,6-dibromophenyl] diacetate	Suspected persistent in the environment Suspected respiratory sensitiser Suspected skin sensitiser	No	–
25	4162-45-2	**TBBPA-BHEE**	4,4′-Isopropylidenebis (2-(2,6-dibromophenoxy)ethanol)	Suspected bioaccumulative Suspected persistent in the environment	No	–
26	25 327-89-3	**TBBPA-BAE** (TBBPA-DAE, TBBPA-AE)	1,1′-Isopropylidenebis [4-(allyloxy)-3,5-dibromobenzene]	Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected toxic for reproduction	No	**1–10 tonnes per year.** Used in polymers.
27	55 205-38-4	**TBBPA-BA**	Tetrabromobisphenol A bisacrylate	No results were found	No results were found	–
28	3072-84-2	**TBBPA-BGE** (TBBPA-DGE, TBBPA GE)	2,2’-[(1-Methylethylidene)bis [(2,6-dibromo-4,1-phenylene)oxymethylene]]bisoxirane	Suspected bioaccumulative Suspected hazardous to the aquatic environment	No	**100–1000 tonnes per year.** Used in building & construction work as well

				Suspected mutagen Suspected persistent in the environment Suspected skin irritant		as plastic products, electronic equipment and vehicles.
29	37 419-42-4	**TBBPA-BP**	Tebrabromobisphenol A bispropanoate	no results were found	No results were found	no results
30	37 853-59-1	**BTBPE**	1,1'-[Ethane-1,2-diylbisoxy]bis [2,4,6-tribromobenzene]	Suspected hazardous to the aquatic environment Suspected persistent in the environment	Yes	–
31	66 710-97-2	**TBBPA-BHEEBA**	(1-Methylethylidene)bis [(2,6-dibromo-4,1-phenylene)oxy-2,1-ethanediyl] diacrylate	Suspected mutagen Suspected persistent in the environment Suspected respiratory sensitiser Suspected skin irritant Suspected skin sensitiser	No	–
32	1 084 889-51-9	**OBTMPI** (OBIND)	Octabromotrimethylphenyl indane	No results were found	No results were found	–
33	21 850-44-2	**TBBPA-BDBPE** (TBBPA-DBPE)	1,1'-(Isopropylidene)bis [3,5-dibromo-4-(2,3-dibromopropoxy)benzene]	No hazards have been classified	PBT assessment: not considered PBT, not bio accumulative or toxic	**1000–10 000 tonnes per year.** Used in polymers, textile and dyes, as well as in water treatment products and pH regulators.
34	32 588-76-4	**EBTEBPI**	N,N′-Ethylenebis (3,4,5,6-tetrabromophthalimide)	No hazards have been classified	Not fulfilling PBT & vPvB criteria: not bio accumulative or toxic but expected to be persistent (in soil).	**100–1000 tonnes per year.** Manufactured for plastic and rubber products, textiles, leather or fur.
35	42 757-55-1	**TBBPS-BDBPE**	Bis [3,5-dibromo-4-(2,3-dibromopropoxy) phenyl] sulphone	Suspected carcinogen Suspected mutagen Suspected persistent in the environment Suspected skin irritant	No	–
36	84 852-53-9	**DBDPE** (BDPE-209, DBDE)	1,1'-(Ethane-1,2-diyl)bis [pentabromobenzene]	May cause long lasting harmful effects to aquatic life	Suspected PBT/vPvB; very persistent Under assessment	**10 000–100 000 tonnes per year.** Used in polymers, adhesives and sealants, coating products, inks, toners and washing & cleaning products. Also used in re-packaging, building & construction work.
37	497 107-13-8	**DBDBE** (BDBE-209)	Decabromodibenzyl ether	No results were found	No results were found	–
38	58 965-66-5	**4′-PeBPOBDE208**	1,2,4,5-Tetrabromo-3,6-bis(pentabromophenoxy)benzene	Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser Suspected toxic for reproduction	No	–
39	34 571-16-9	**HCTBPH** (Dec 604)	1,2,3,4,7,7-Hexachloro-5-(tetrabromophenyl) bicyclo [2.2.1]hept-2-ene	Suspected bioaccumulative Suspected persistent in the environment Suspected skin sensitiser	No	–
40	3322-93-8	**DBE-DBCH** ((α-, β-) TBECH, TBEC))	1,2-Dibromo-4-(1,2-dibromoethyl) cyclohexane	Suspected carcinogen Suspected hazardous to the aquatic environment Suspected mutagen Suspected persistent in the environment Suspected skin irritant Suspected skin sensitiser	No	–
41	3194-57-8	**TBCO** ((α-, β-)TBCO)	1,2,5,6-Tetrabromocyclooctane	No harmonized classification, but C&L inventory: Harmful if swallowed or inhaled Harmful in contact with skin	No	–

(*continued on next page*)

Table 1 (*continued*)

	CAS-no.	NBFR practical abbreviation	Name	REACH ECHA Annex Inventory III [a]	PBT/vPvB assessment [b]	Use or Production
				Causes skin irritation Causes serious eye irritation May cause respiratory irritation		
42	51 936-55-1	**DBHCTD** (HCDBCO)	7,8-Dibromo-1,2,3,4,11,11-hexachloro-1,4,4a,5,6,7,8,9,10,10a-decahydro-1,4-methanobenzocyclooctene	Suspected bioa ccumulative Suspected carcinogen Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin irritant Suspected skin sensitiser Suspected toxic for reproduction	No	–
43	25 495-98-1	**HBCYD**	Hexabromocyclodecane	Suspected of damaging fertility or the unborn child May cause harm to breast-fed children Very toxic to aquatic life Very toxic to aquatic life with long lasting effects	PBT and R (suspected Toxic for Reproduction)	**1000–10 000 tonnes per year**
44	57 829-89-7	**DBP-TAZTO**	1-(2,3-Dibromopropyl)-3,5-diallyl-1,3,5-Triazine-2,4,6(1H,3H,5H)-trione	No results were found	No results were found	–
45	75 795-16-3	**BDBP-TAZTO**	1,3-Bis(2,3-dibromopropyl)-5-allyl-1,3,5-triazine- 2,4,6(1H,3H,5H)-trione	No results were found	No results were found	–
46	52 434-90-9	**TDBP-TAZTO**	1,3,5-Tris (2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione	Suspected carcinogen Suspected mutagen Suspected persistent in the environment Suspected skin irritant	No PBT assessment	**1–10 tonnes per year.** Used in polymers.
47	25 713-60-4	**TTBP-TAZ**	1,3,5-Triazine, 2,4,6-tris(2,4,6-tribromophenoxy)-	No hazards have been classified	PBT assessment: under development	**1000+ tonnes per year.** Used for plastic and electronic products and optical equipment.
48	19 186-97-1	**TTBNPP** (TTBNP)	Tris [3-bromo-2,2-bis(bromomethyl)propyl] phosphate	No hazards have been classified	Yes	**10+ (10–100) tonnes per year.** Used for plastic and electronic products and optical equipment.
49	126-72-7	**TDBPP**	Tris (2,3-dibromopropyl) phosphate	Suspected carcinogen Suspected hazardous to the aquatic environment Suspected mutagen Suspected persistent in the environment Suspected skin irritant	Yes	–
50	3296-90-0	**DBNPG** (DBPT)	2,2-Bis(bromomethyl)propane-1,3-diol	Suspected of causing genetic defects Suspected of causing cancer	No	**100–1000 tonnes per year.** Used in polymers and for thermoplastic manufacturing. Also used in building & construction work.
51	1522-92-5	**TBNPA** (TBPT)	2,2,2-Tris (bromomethyl)ethanol, FR 1360, FR 513	Causes serious eye irritation Harmful if swallowed, in contact with skin or if inhaled May cause respiratory irritation	No results	–
52	106-41-2	**4-BP**	4-Bromophenol	Suspected acutely toxic via the oral route Suspected bioaccumulative Suspected carcinogen Suspected hazardous to the aquatic environment Suspected mutagen Suspected persistent in the	No	–

				environment Suspected skin irritant		
53	99 717-56-3	**BATE**	2-Bromoallyl 2,4,6-tribromophenyl ether	No results were found	No results were found	–
54	87-84-3	**PBCC**	1,2,3,4,5-Pentabromo-6-chlorocyclohexane	Suspected bioaccumulative Suspected carcinogen Suspected hazardous to the aquatic environment Suspected mutagen Suspected persistent in the environment	No	–
55	39 569-21-6	**TBCT** (TBoCT)	2,3,4,5-Tetrabromo-6-chlorotoluene	Suspected bioaccumulative Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser	No	–
56	608-90-2	**PBBZ**	1,2,3,4,5-Pentabromobenzene	Causes serious eye irritation May cause long lasting harmful effects to aquatic life	No	–
57	2039-86-3	**3-bromostyrene**	3-Bromostyrene	Suspected carcinogen Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected respiratory sensitiser Suspected skin irritant	No	–
58	61 262-53-1	**EBP**	1,1'-[Ethane-1,2-diylbisoxy]bis [pentabromobenzene]	Suspected hazardous to the aquatic environment Suspected persistent in the environment Suspected skin sensitiser	No	–
59	27 581-13-1	**Tetrabromobenzoic acid**	2,3,4,5-Tetrabromobenzoic acid	No results were found	No results were found	–
60	13 810-83-8	**Tetrabromophthalic acid**	Tetrabromobenzene-1,2-dicarboxylic acid	Causes serious eye irritation Causes skin irritation and May cause respiratory irritation	No	–
61	608-33-3	**2,6-DBP** (26DBP)	2,6-Dibromophenol	Suspected hazardous to the aquatic environment Suspected mutagen Suspected persistent in the environment Harmful if swallowed and if inhaled Harmful in contact with skin	No	–
62	30 554-73-5	**TrBTrCCH**	Tribromotrichlorocyclohexane	Suspected carcinogen Suspected persistent in the environment Suspected skin irritant	No	–
63	14 400-94-3/36 313-15-2	**TetraBRP**	Tetrabromophenol	No information on substance card	No information on substance card	–

[a] **ECHA Annex Inventory III:** the annex III is an advisory tool on a substance its hazardous effect, toxicity and bio accumulatively. The inventory indicates concerns. 'Suspected carcinogen' does not mean the substance *is* carcinogen, (more) proof would be needed to arrive at such a conclusion (ECHA, 2019).

[b] **PBT/vPvB assessment:** the PBT assessment list includes substances that have been submitted to a PBT/vPvB assessment (hazard assessment for PBT/vPVB properties: substances persisting for long period of time in the environment and/or have a high bio accumulative potential). PBT: Persistence, Bioaccumulation and Toxicity and vPvB: very persistent and very bioaccumulative (ECHA, 2019).

Table 2
Data on NBFRs found in consumer goods: medians (μg/g), location, type of sampled material and ref.

	Median (μg/g)	Location (Geography)	Sampled material	Reference
EH-TBB	48.07	South-Africa	Motherboard 1	Nkabinde et al. (2018)
	17.32	South-Africa	Flat screen monitor 1	Nkabinde et al. (2018)
	110.64	South-Africa	CRT monitor 1	Nkabinde et al. (2018)
	92.64	South-Africa	Keyboard 1	Nkabinde et al. (2018)
	51.33	South-Africa	Plastic chair	Nkabinde et al. (2018)
	672.54	South-Africa	Foam chair	Nkabinde et al. (2018)
	260	South-Africa	Biltong machine	Nkabinde et al. (2018)
	87.6	South-Africa	Plastic chair	Nkabinde et al. (2018)
	39.5	South-Africa	Leather chairs	Nkabinde et al. (2018)
	33.1	South-Africa	Flat screen monitor 2	Nkabinde et al. (2018)
	21	South-Africa	Motherboard 2	Nkabinde et al. (2018)
	164	South-Africa	Keyboard 2	Nkabinde et al. (2018)
	51.9	South-Africa	Cooling fan 1	Nkabinde et al. (2018)
	29.3	South-Africa	Motherboard 4	Nkabinde et al. (2018)
	9542[a]	USA	Foam pit	La Guardia and Hale, 2015
HBB	180	China	Computer casing	Sun et al. (2018)
	468	China	Sound insulation cotton	Sun et al. (2018)
	165	China	Decorative laminate	Sun et al. (2018)
	0.76	USA	Foam (from car seats from USA, Canada, China)	Wu et al., 2018
	0.13	USA	Fabric (from car seats from USA, Canada, China)	Wu et al., 2018
	0.23	USA	Composite (from car seats from USA, Canada, China)	Wu et al., 2018
	0.031[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
BEH-TEBP	128	China	New carpet	Sun et al. (2018)
	14.01	South-Africa	Motherboard 1	Nkabinde et al. (2018)
	18.19	South-Africa	Flat screen monitor 1	Nkabinde et al. (2018)
	59.32	South-Africa	Plastic chair	Nkabinde et al. (2018)
	62.31	South-Africa	Printer 2	Nkabinde et al. (2018)
	34.31	South-Africa	Motherboard 4	Nkabinde et al. (2018)
	3578[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
BTBPE	496	China	Computer casing	Sun et al. (2018)
	680	China	Decorative laminate	Sun et al. (2018)
	293	China	PVC floor	Sun et al. (2018)
	31.93	South-Africa	Motherboard 1	Nkabinde et al. (2018)
	13.06	South-Africa	Flat screen monitor 1	Nkabinde et al. (2018)
	425.18	South-Africa	CRT monitor 1	Nkabinde et al. (2018)
	50.7	South-Africa	Keyboard 1	Nkabinde et al. (2018)
	430.72	South-Africa	Plastic chair	Nkabinde et al. (2018)
	210.17	South-Africa	Foam chair	Nkabinde et al. (2018)
	46.72	South-Africa	Book shelves	Nkabinde et al. (2018)
	215.55	South-Africa	Biltong machine	Nkabinde et al. (2018)
	78.94	South-Africa	Plastic chair	Nkabinde et al. (2018)
	278.65	South-Africa	Flat screen monitor 2	Nkabinde et al. (2018)
	42.87	South-Africa	Printer 2	Nkabinde et al. (2018)
	1066.4	South-Africa	Motherboard 2	Nkabinde et al. (2018)
	151.1	South-Africa	CRT monitor 2	Nkabinde et al. (2018)
	1402	South-Africa	Keyboard 2	Nkabinde et al. (2018)
	237.45	South-Africa	Motherboard 3	Nkabinde et al. (2018)
	107.79	South-Africa	Cooling fan 1	Nkabinde et al. (2018)
	83.09	South-Africa	Cooling fan 2	Nkabinde et al. (2018)
TBP-AE	173	China	Sound insulation cotton	Sun et al. (2018)
	183	China	Circuit board	Sun et al. (2018)
	17[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
TBP	29[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
PBEB	0.012[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
PBT	16[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
TBP-DBPE	0.093	USA	Fabric (from car seats from USA, Canada, China)	Wu et al., 2018
	0.28	USA	Fabric (from car seats from USA, Canada, China)	Wu et al., 2018
	63[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
TBBPA-BAE	0.4[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
DBDPE	284	USA	Foam (from car seats from USA, Canada, China)	Wu et al., 2018
	123	USA	Fabric (from car seats from USA, Canada, China)	Wu et al., 2018
	3.4[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)
DBHCTD	66	China	Decorative laminate	Sun et al. (2018)
TDBP-TATZO	10 000	Japan	Curtain	Miyake et al. (2017)
TTBP-TAZ	0.01–0.8**	Netherlands	Electrical power boards and adaptors	Ballesteros-Gómez et al., 2014Ballesteros-Gómez et al., 2014
	0.06, 1.9**	Netherlands	Television	Ballesteros-Gómez et al., 2014Ballesteros-Gómez et al., 2014
	0.3, 0.6**	Netherlands	Other household appliances	Ballesteros-Gómez et al., 2014Ballesteros-Gómez et al., 2014
BATE	2[a]	Germany	Dishcloth (ng/dishcloth)	Gallistl et al. (2017)

[a] Mean instead of median. ** Concentration (% w/w). Weight dishcloth varies between 8.24 and 32 g.

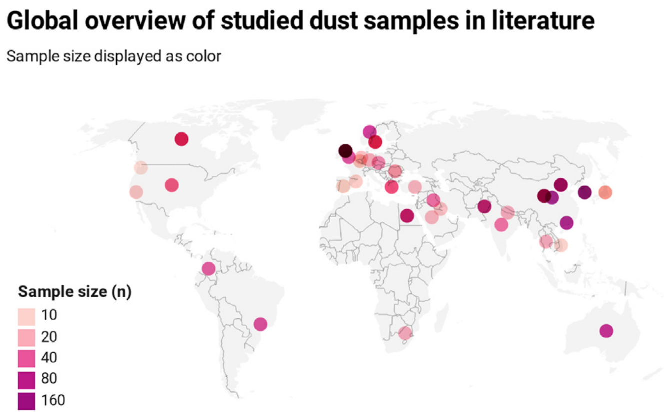

Fig. 2. Global overview of studied dust samples in the literature. Sample size is indicated by a gradual color scale; the color of the dot gets darker with larger sample size sets. [interactive map: https://datawrapper.dwcdn.net/LNVGe/6/]. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

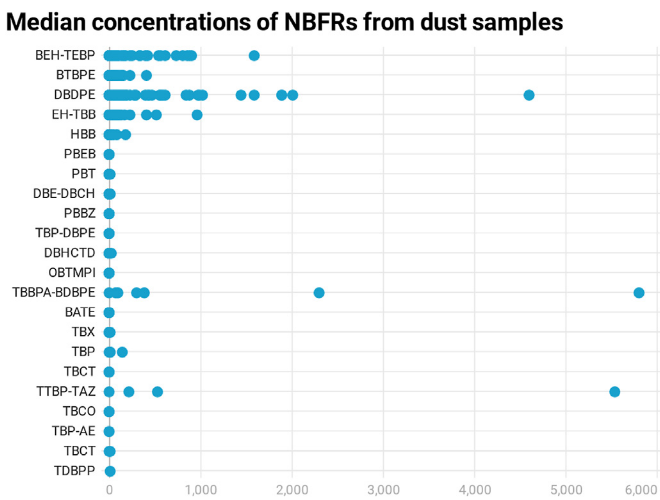

Fig. 3. Overview of median concentrations of NBFRs (ng/g) in dust sample measurements. Range indoor dust: 0.001–6000 ng/g. The graph includes a total of 382 dust samples. The dots near zero are numerous points of multiple measurements between 0.001 and 2 ng/g. To view online and to hover over measurements to show exact numbers, go to [https://datawrapper.dwcdn.net/Og5Ep/1/].

most of the other BFR concentrations, suggesting its dominance at the (Chinese) market. Sahlström et al. (2015) confirmed that DBDPE can exceed legacy BFR concentrations in dust. They also reported a first time detection of TBB and TBPH in Swedish house dust. A large study in Melbourne, Australia, also reported high concentrations of DBDPE (1600–1900 ng/g) (McGrath et al., 2018). Earlier studies conducted by Sahlström et al. (2015) and Wang et al. (2010) already observed these higher concentrations of DBDPE. Studies carried out in Belgium (Ali et al., 2011), USA (Stapleton et al., 2008) and Germany (Fromme et al., 2014) suggest lower levels of DBDPE.

High DBDPE concentrations in China are possibly the result of the more frequent use of DBDPE compared to other countries (Wang et al., 2018). A study from Bu et al. (2019) confirms this hypothesis: the dominant NBFR was DBDPE. As the detection frequency seems to increase, they emphasize the need for further investigations of NBFRs in microenvironments (Bu et al., 2019). According to a study of Kuang et al. (2016) in the UK, concentrations of DBDPE have significantly risen and concentrations of decaBDE significantly fallen. The results from different microenvironments in homes show a lower uptake of NBFRs in dust in kitchens, supposedly because of higher humidity and use of different BFRs in kitchen appliances, and higher emissions in bedrooms and living rooms (Kuang et al., 2016).

Almost half of the studies show median concentrations of DBDPE of 120–881 ng/g (Qi et al., 2014; Sun et al., 2018; Cequier et al., 2014; Dodson et al., 2012; Tao et al., 2016; Sahlström et al., 2015; Persson et al., 2019; Khairy and Lohmann, 2018; Venier et al., 2016; McGrath et al., 2018; Newton et al., 2015; Niu et al., 2019; Reche et al., 2019; Fromme et al., 2014; Al-Omran and Harrad, 2016; Wang et al., 2018; Bu et al., 2019; Ali et al., 2011) and three studies show a high value of 1600–4600 ng/g (Ali et al., 2011; McGrath et al., 2018; Tang et al., 2019).

3.2.3. Other observations

Concentrations of most NBFRs were higher in urban samples than in rural samples. The same was true for public spaces versus homes (Qi et al., 2014). This may be caused by stricter flame retardancy legislation for public spaces than for homes. Another study from Pakistan suggested higher concentrations of NBFRs in industrial areas compared to rural areas (Khan et al., 2016). Both studies are in line considering the more heavy application of NBFRs, e.g. in electronics and furniture, in public and urban spaces (Qi et al., 2014). Also Sun et al. (2018) state that the sum of electrical applications, use of building material and ventilation significantly influences concentrations of NBFRs (Sun et al., 2018). Qi et al. (2014) suggest two possible reasons for the perceived spatial distribution in their measurements: high room temperatures and less air circulation contribute to higher concentrations of NBFRs in dust and air samples (Qi et al., 2014). Persson et al. (2019) highlight the differences in concentrations, and in compounds, per dust and air sample. They suggest cleaning routines and ventilations systems may contribute to these variations. They emphasize the importance of emissions (leaching) tests for equipment, furniture, building materials and consumer goods are important in order to be able to specify in detail the sources of the (N)BFRs. Additionally, they suggest to include an inventory list of goods and materials per room for each measurement. This could potentially provide valuable information on emissions sources of NBFRs (Persson et al., 2019).

Hassan and Shoeib (2015) reported lower levels of non-PBDE BFRs and PBDEs in Egyptian dust compared to other countries. They suggest that the less strict fire regulations are related to these findings (Hassan and Shoeib, 2015). A research conducted by Khairy et al. in Alexandria (Egypt) in 2018 reported the same concentration range. However, concentrations of PBP, PBEB and DBHCTD were also reported (Khairy and Lohmann, 2018). BEH-TEBP was not analyzed, although it was found in a previous study of Hassan and Shoeib (2015). Niu et al. (2019) make a specific distinction between floor dust (FD) and elevated surface dust (ESD), which both need to be measured and assessed. Also other studies highlight this distinction of these two types of dust: median concentrations of ESD being significantly higher than FD (Al-Omran and Harrad, 2016). On the basis of the results of Newton et al. (2015), they suggest that the more volatile NBFRs (e.g. Pentabromotoluene (PBT) and 4-(1,2-Dibromoethyl)-1,2-dibromocyclohexane (DBE-DBCH)) would be more frequently present in air and less volatile NBFRs, such as DBDPE and BEH-TEBP, more frequently present in dust (Newton et al., 2015).

3.3. NBFRs in indoor air

Studies on the ‘indoor environment’ often combine indoor dust and air measurements. However, significantly fewer articles were found on indoor air compared to indoor dust. More data is needed

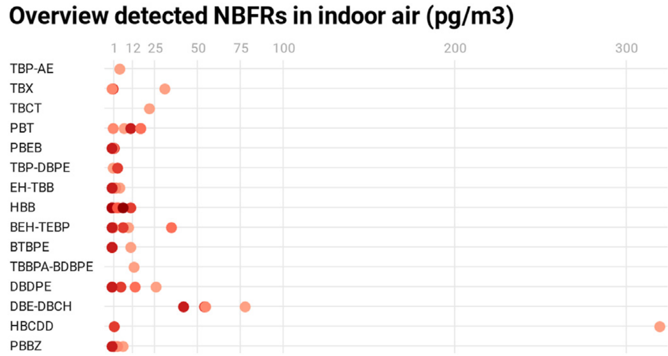

Fig. 4. Overview of detected NBFRs in indoor air (pg/m^3). *HBCDD is a legacy BFR, here given for comparison.

to enable the determination of a spatial or temporal trend. Comparison to outdoor air is also often included in the research. Data on 443 samples from different studies indicates the presence of 19 NBFRs in indoor air/ventilation air in various spaces (see Fig. 4). Indoor air was measured in homes, offices, cars, classrooms, gyms and an e-waste recycling facility.

Reche et al. (2019) shows higher concentrations of NBFRs than legacy BFRs in indoor air in Spanish offices, suggesting this could be the result of policy intervention: replacement of legacy BFRs by NBFRs in electronic equipment. Outdoor air on the contrary showed higher concentrations of PBDEs compared to NBFRs. They suggest these higher concentrations are a consequence of the high abundance of PBDEs in recycling facilities and landfills (Reche et al., 2019). In a study from Sweden focusing on indoor air, outdoor air and ventilation air, eight different NBFRs were found and although in all samples these were detected, concentrations in indoor air were much higher than in outdoor air (Newton et al., 2015). Research at a Canadian e-waste recycling facility indicated the presence of one novel BFR, TTBP-TAZ, in indoor air (also in dust, as indicated in section 4.1) (Guo et al., 2018). A study collecting samples from three different countries (USA, Canada and Czech-Republic) found contamination of EH-TBB, HBB, BEH-TEBP, BTBPE and DBDPE for all countries, with concentrations varying between 0.038 and 6.4 pg/m^3. Additionally, only in USA-samples concentrations of TBX and PBEB (0.044 and 0.016 pg/m^3 respectively) were detected. They found in general the highest levels of FRs in the USA and the lowest in Czech Republic, and suggest this trend reflects the FRs market (Venier et al., 2016).

Vojta et al. (2017) found an increase of almost 900% in NBFRs in indoor air when computers were switched on and operating. This result suggests that the presence of some NBFRs is strongly linked to electronic products used indoors (Vojta et al., 2017).

3.4. NBFRs in food

3.4.1. Food (general)

Uptake of NBFRs via diet is an important exposure route. Sahlström et al. (2015) detected several NBFRs in fish in concentrations that equal those of HBCDD and PBDEs. This does not only emphasize the need for more measurements of NBFRs in food, but foremost tells us that the replacements of restricted FRs have already reached the human food chain (Sahlström et al., 2015). A study from Wang et al. (2018) supports this finding, stressing food consumption as an important pathway for BFR uptake for the population of Beijing (Wang et al., 2018).

Compared to other products, the highest NBFR concentrations are often found in fish (products), mainly because of their bioaccumulative potential (Poma et al., 2018). The exception was BEH-TEBP, which was mainly detected in eggs and dairy products. However, due to the higher consumption of it, meat appears to be the main contributor to NBFR levels in humans, followed by fish (Tao et al., 2016; Shi et al., 2018). The highest NBFR intake was reported for DBE-DBCH, 14 ng/day for adults, in a study on various UK food items (Tao et al., 2017). Shi et al. (2016) found DBDPE to be predominant in Chinese samples (9.03 ng/g lipid weight (lw) in food and 8.06 ng/g lw in human milk). The latter indicated a shift in production and usage patterns between PBDEs and NBFRs, especially DBDPE. With the restriction of PBDEs and HBCDDs, consumption of NBFRs is increasing (Shi et al., 2016).

A large study on 600 French foodstuff samples demonstrated the presences of PBT, PBBz and HBB in various food groups. The concentrations are in general lower compared to concentrations of legacy BFRs (Vénisseau et al., 2018). Obviously, this may change in time, as the NBFRs are still being used whereas the legacy BFRs have been banned. Poma et al. (2018) found high concentrations of HBCDD, but very low, non-quantifiable levels of HBB, EH-TBB and BTBPE in various food items such as potatoes, milk and deserts.

A recent study on vegetables from China (Zhejiang Province) indicated the presence of six NBFRs (HBB, EH-TBB, TBP-AE, BTBPE, DBDPE and DBHCTD). Research on both plastic greenhouse and conventional vegetable cultivation (CVC) showed significantly higher NBFR concentrations in greenhouse vegetables. Consumption of these leads to a significantly higher intake risk (Sun et al., 2019). The use of plastic greenhouses (opposed to glass greenhouses and CVC) has expanded worldwide in recent years. The socioeconomic benefits being, among others, high yields, high quality vegetables and its relative cheapness. However, disadvantages have been brought forward as well: generation of large amounts of plastic waste and higher greenhouse-gas emissions compared to CVC (Chang et al., 2013). For plastic greenhouse tomatoes, the estimated daily intake (EDI) was 2409 (±289) ng/day compared to 760 (±91) ng/day for conventional tomatoes. EDI of plastic greenhouse cucumbers was 3114 ng/day compared to 1521 (±56) for conventional cucumbers. They concluded that plastic greenhouses may not be the best choice for vegetable production. To reduce accumulation of (N)BFRs, future greenhouse should be optimized in terms of reducing the vegetable growth period as much as possible (Sun et al., 2019). Glass greenhouses may be a sound alternative.

3.4.2. Seafood

Consumption of seafood is a major dietary exposure route for environmental contaminants. In 2008, the European Union adopted the Marine Strategy Framework Directive (MSFD) (2008/56/EC) including monitoring programs on chemical contaminants in seafood. The MSFD target group 9 established in 2010 BFRs to be taken up in the list of priority contaminants (Swartenbroux et al., 2010). During the past years more studies have been carried out on (N)BFRs in seafood but still only a few reports cover the susceptibility of aquatic organisms to these substances. Legacy BFRs, and specifically PBDEs, are often found present in seafood. In an extensive study on European market seafood species, PDBEs were detected in 85% of the samples, concentration varying between 0.017 and 17.3 ng/g ww (Aznar-Alemany et al., 2017). In a recent study on Norwegian seafood, levels up to 11.4 ng/g for HBCDD were found (Nøstbakken et al., 2018). A review on BFRs and seafood by Cruz et al. (2015) found 79 articles confirming concentrations of HBCDD were found in seafood, concentrations even reaching 11 140 ng/g (Chen et al., 2011). The same study of Cruz et al. (2015) found 229 research articles on seafood contaminated with PDBEs, including very high concentrations from 16 000 ng/g to 108 000 ng/

g (Echols et al., 2013; Xiaofei et al., 2009). NBFRs are not as frequently present. A reason could be that they have not been studied as often. However, their concentrations should not be neglected (Aznar-Alemany et al., 2017; Trabalón et al., 2017). Li et al. (2019) published data demonstrating the wide occurrence of NBFRs in globally collected fishmeal samples. These findings do raise concern regarding the use of NBFRs. Animal products pose a higher risk of NBFR contamination as lipophilic compounds tend to accumulate in animal tissue (Li et al., 2019).

In a study from Catalonia, Spain, (N)BFRs in samples of ten different fish species were analyzed. Three NBFRs were studied. HBB was identified in most samples, whereas PBEB and DBDPE were not detected at all (Trabalón, 2017).

Human uptake of NBFRs from seafood can be relatively high due to their occurrence in seafood species. The process of cooking can concentrate flame-retardants, but most probably because of water evaporation (Aznar-Alemany, 2017; De Boer et al., 2013). Another study showed decreased (N)BFR bio accessibility in culinary treated seafood compared to raw seafood (Alves et al., 2017). However, a study on cooking and frying eel (with PCBs and OCPs) indicated that these processes do not lead to lower concentrations. Cooking had no significant effect at all. During frying 19% of PCBs and OCPs moved into the frying butter (De Boer et al., 2013). Further research should be done on NBFR contamination and risk associated with cooked and processed seafood.

3.4.3. Human milk and exposure

In both food and human milk, levels of NBFRs (BTBPE, DBDPE, PBT, HBB and DPTE) appear to be increasing 4, while levels of legacy BFR TBBPA also appear to be increasing (Shi et al., 2018). In China, relatively high levels of DBDPE found in human diet and human milk show that the Chinese population is continuously exposed to high DBDPE concentrations (Shi et al., 2016, 2018). A total daily intake of NBFRs via human milk was estimated at 29.3 ng/kg bw/day (Shi et al., 2016). In the UK, DBE-DBCH and EH-TBB seem to be of highest concern as regards diet exposure. High levels of BEH-TEBP and DBDPE were also present, but these are mainly taken up by dust ingestion (Tao et al., 2017). This study also included human milk samples. Contrary to Shi et al. (2018), Tao et al. (2017) indicated that significant changes in temporal trends for legacy FRs and NBFRs are not observed for human milk. The response in human bodies to the change in the use of these chemicals may probably need more time.

4. Discussion: NBFRs of concern

The NBFRs produced in high volumes and those which pose certain concern are discussed below. Table 3 lists their concerns in regard to their toxicity, hazardousness and impact to the environment (ECHA, 2019). Further research on their environmental occurrence, persistence and fate as well as their toxicity is therefore needed. Many NBFRs are not included in sample measurements and/or are not studied (28) (Fig. 5). Measuring NBFRs is an analytical challenge, in terms of generalized good QA/QC and pure standards. In an interlaboratory study on novel FRs, differences in results may be caused by differences in the analytical methods used, such as variation in method detection limits, matrix effects and/or validation of method using standard reference materials (Melymuk et al., 2018).

A handful of NBFRs (EH-TBB, BEH-TEBP, BTBPE and DBDPE) urgently need more research in terms of risk assessment and toxicological effects on humans and the environment. These important replacements of legacy BFRs are nowadays used in large quantities and restrictions seem badly needed to counter uncontrolled use and reduce health risks for humans (de Boer and Stapleton, 2019).

4.1. TBBPA derivatives

In 2008, TBBPA was approved by the EU after an eight-year risk assessment. TBBPA potentially has endocrine disrupting and toxic effects on aquatic life and human reproduction and development (DEPA Danish Environmental Protection Agency, 2015). Some studies highlight a potential alternating effect of TBBPA on thyroid hormone levels, however, this has not been proven (Yang et al., 2016; Lai et al., 2015). According to a report from one of the member states: "Lack of data for the TBBPA derivatives and TBBPS is also objective for further risk management" (DEPA Danish Environmental Protection Agency, 2014). For example, no results were found for TBBPA-BP in ECHA. However, according to a report of the Danish Environmental Protection Agency this TBBPA derivative, based on QSAR modelling, has similar geno-toxicity, carcinogenicity and skin sensitization profiles to TBBPA-BOAc (Wedebye et al., 2016), which according to ECHA is 'suspected persistent in the environment, suspected respiratory sensitiser and suspected skin

Table 3
High median concentration NBFRs (measurements above 500 ng/g) that were found in the literature and medium high median concentrations (10 ng/g − 500 ng/g). *Indoor air concentration (pg/m^3).

High median concentrations (>500 ng/g)	Medium median concentrations (10–500 ng/g)
All are suspected to be hazardous to aquatic life and suspected to persist in the environment	
EH-TBB	**DBE-DBCH***
Potentially an endocrine disruptor	Suspected to be carcinogen and mutagen
Not clearly taken up in ECHA!	
*Only as reaction mass of BEH-TEBP***	
BEH-TEBP	**TBBPA-BDBPE**
Wide dispersive use	Potentially bio-accumulative and toxic
Marked as low-volume chemical, this is outdated!	Potentially an endocrine disruptor
Potentially an endocrine disruptor	
Other hazard-based concerns	
**Very toxic to aquatic life	
**Very toxic to aquatic life with long lasting effects	
DBDPE	**PBT & HBB**
Potentially an endocrine disruptor	Suspected to be bio-accumulative
May cause long lasting harmful effects to aquatic life	
BTBPE	**TBX***
Potentially an endocrine disruptor	Suspected to be bio-accumulative
Suspected to be carcinogen and mutagen	Suspected to be toxic for reproduction

**In ECHA found as Bis(2-ethylhexyl) 3,4,5,6-tetrabromophthalate; reaction mass of: 2-ethylhexyl 2,3,4,5-tetrabromobenzoate.

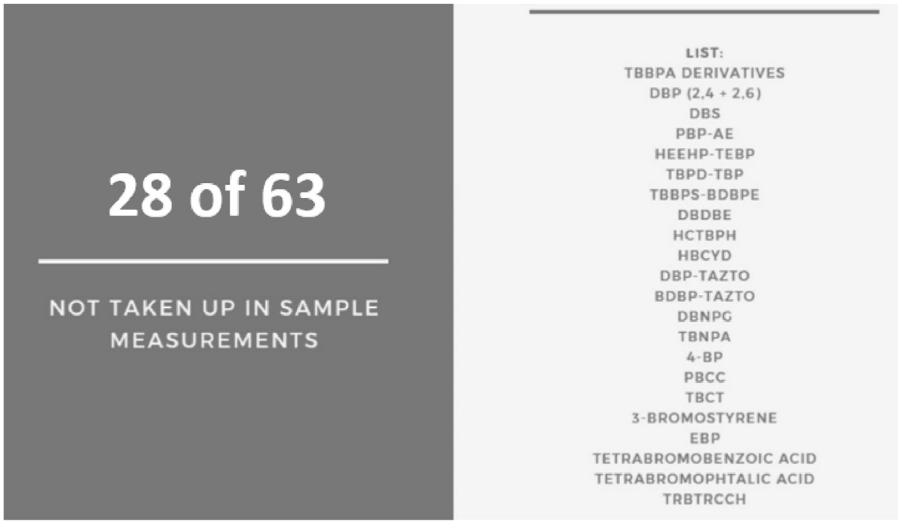

Fig. 5. List of NBFRs which were not included in sample measurements. TBBPA derivatives are: TBBPA-BME, TBBPA-BOAc, TBBPA-BHEE, TBBPA-BA, TBBPA-BGE, TBBPA-BP, TBBPA-BHEEBA (Bergman et al., 2012).

sensitiser' (ECHA, 2020). Little research is done on TBBPA derivatives (eight have been identified), not on their occurrence nor toxic properties. With current knowledge on TBBPA, the lack of data on TBBPA derivatives should be a priority.

4.2. EH-TBB

No results were found by ECHA. There is, however, an urgent need for data, risk assessment and regulatory advice. However, results were found on BEH-TEBP with reaction mass of EH-TBB (Bis(2-ethylhexyl) 3,4,5,6-tetrabromophthalate; reaction mass of: 2-ethylhexyl 2,3,4,5-tetrabromobenzoate). The hazardous classification stated 'this substance is very toxic to aquatic life, is very toxic to aquatic life with long lasting effects' (ECHA, 2020). Different legislation is implemented, the Worker Protection-Hazardous (98/24) (Directive 98/24/EC), Dangerous Substances Eco-Labels (Reg. 66/2010/EC), protection of Young People at the Workplace (Directive 94/33/EC), and Hazardous Waste Properties (Directive, 2008/98/EC).

EH-TBB is a potentially endocrine disrupting chemical. Knudsen et al. (2016) provided a risk assessment for dermal exposure. EH-TBB is absorbed by the human skin and therefore a potential risk, especially for children and pregnant women (Knudsen et al., 2016). Bioaccumulation of EH-TBB does not seem to be as high compared to other NBFRs such as BTBPE (log K_{ow} 7.1 vs. 8.31) (Roberts et al., 2012). However, accumulation in skin tissue has been reported (Abdallah et al., 2019; Frederiksen et al., 2016). There is also concern regarding the metabolism of EH-TBB. It may form 2,3,4,5-tetrabromo benzoic acid (TBBA), which has an estimated log-K_{ow} value of 8.8, and toxicological implications are largely unknown (Roberts et al., 2012; Dishaw et al., 2014). According to Hays and Kirman (2017), biomonitoring data of EH-TBB and its metabolite TBBA are scarce. It is highly important that EH-TBB will be registered by the European Chemicals Agency.

4.3. BEH-TEBP

BEH-TEBP is used in many different articles, such as constructing materials, toys, electronic equipment and packaging material (ECHA, 2019). The EU approved classification (ATP01) stated for BEH-TEBP with reaction mass of EH-TBB (which is a different datasheet than BEH-TEBP) 'this substance is very toxic to aquatic life, is very toxic to aquatic life with long lasting effects and may cause an allergic skin reaction'. Its production data is confidential (ECHA, 2020). The chemical sheet of BEH-TEBP itself states ECHA is carrying out a PBT/vPvB assessment, although a decision has been deferred because "it is a low production volume chemical". This is, however, rather outdated (and it is confusing to have two different chemical sheets). Nowadays it is a high production volume chemical (Nacci et al., 2018). At the moment, Sweden is carrying out an assessment. BEH-TEBP is a potential endocrine disruptor and there are concerns regarding its wide use, toxicity, persistence and bioaccumulative potential (ECHA, 2019).

4.4. DBDPE

The datasheet for DBDPE states it 'may cause long lasting harmful effects to aquatic life' (ECHA, 2020). According to its registration dossier, DBDPE is very persistent in water, sediment and soil, but not bio-accumulative nor toxic. Its physico-chemical properties are presumably resembling decaBDE. It also has a very low water solubility of circa 0.72 μg/L (ECHA, 2019). According to Wang et al. (2019) DBDPE seems to be less toxic than BDE-209, but it is potentially an endocrine disruptor. Recently, research indicated a potential harmful effect of DBDPE on the cardiovascular system (Jing et al., 2019). More research is therefore urgently needed. Since the beginning of this research things have changed. The Canadian Government has proposed, at the end of August 2019, to include DBDPE in the List of Toxic Substances (Canadian Environmental Protection Act, 1999). REACH still proposes no hazards for DBDPE. However, DBDPE is suspected to be PBT and currently under PBT/vPvB assessment (Persistent, Bioaccumulative and Toxic and very Persistent and very Bioaccumulative), results are soon to be expected (ECHA, 2020).

4.5. BTBPE

BTBPE is currently one of the most commonly used BFRs, yet no hazards have been classified. However, it is suspected hazardous to the aquatic environment as well as suspected to persist in the environment (ECHA, 2019). Different studies have already indicated its environmental persistence and its ability to bio accumulate in

Table 4
Identified research gaps.

Research gaps	
Unknown occurrence of many NBFRs	Research targeting *all* NBFRs
	Data on production (volumes) of all NBFRs. More transparency in (industrial) data
	Development and optimization analytical methods and internal standards NBFRs
	The synthesis of native NBFR to make analytical standard solutions commercially available
Environmental impact NBFRs	Data on environmental occurrence of NBFRs
	Data on environmental impact and fate of NBFRs
Human exposure	Data on emission sources of NBFRs, studies on (consumer) goods
Toxicity and cumulative effects	Studies on toxicity and (bio)accumulative effects of many NBFRs, also in order to establish legislation
Concerns	High concentrations: EH-TBB, BEH-TEBP, DBDPE, BTBPE
	High consumption: TBBPA (and a severe research gap on TBBPA derivatives)
	Overall effect of exposure to combined (N)BFRs
	Regrettable substitution

the aquatic environment (de Wit et al., 2010; Vorkamp and Riget, 2014; de Jourdan et al., 2014). Giraudo et al. (2017) suggested “that BTBPE impacted molecular pathways involved in oxidative stress and endocrine disruption in trout” (pg. 47). Toxic effects and environmental fate should definitely be further studied.

5. Conclusions

This study collected recent information on 63 NBFRs, their occurrence in indoor dust, air, consumer goods and food. It also includes a list of NBFRs and their EU registration and (potential) risks. The increasing application of NBFRs calls for more research on their environmental fate and toxicity, including research on analytical methods measuring these compounds. Table 4 indicates various research gaps regarding occurrence and concerns of NBFRs.

It became clear that the indoor environmental occurrence of many (28) NBFRs has not been studied at all (Fig. 5). This is also likely due to the analytical challenges in measuring these compounds. For example, the occurrence of dibromoneopentyl glycol (DBNPG) and tris(2,3-dibromopropyl) phosphate (TDBPP) are not or very little studied. However, warnings indicate they cause cancer and can have genetic effects. Research on the occurrence and spatial and temporal trends of *all* NBFRs is a clear priority. The lack of proper analytical methods may have contributed to the scarcity of data. There have been no maximum tolerance levels set for NBFRs because of limited data on their toxicity and other characteristics.

Measurements in various micro-environments show the presence of and human exposure to NBFRs in indoor spaces. Research on NBFRs in dust clearly indicates substantial levels of EH-TBB, BEH-TEBP, DBDPE, BTBPE, which are major replacements of Penta-BDE and Deca-BDE. In some dust and food measurements, DBDPE even exceeded concentrations of legacy BFRs. Alarmingly, EH-TBB, BEH-TEBP and DBDPE may be very toxic to aquatic life with long lasting effects and potentially are endocrine disruptors. BTBPE is suspected to be carcinogen and mutagen. Little research is done on TBBPA derivatives, neither on their occurrence nor on their toxic properties. Furthermore, in many studies high concentrations of TBBPA were detected. Nowadays, TBBPA makes up 60% of the total BFR market. Although TBBPA is a chemically bonded FR and cannot easily be released into the environment of consumer goods, it is persistent and will finally end up in the environment. Of the high quantities in which TBBPA is used pose questions of its possible environmental and health effects. In addition, we know very little on possible cumulative effects of all (N)BFRs.

Due to the restrictions on legacy BFRs, the use of NBFRs is most likely to increase. Due to health risks and effects on the environment, more legislation on the use of most abundant replacements of legacy BFRs may be important. Banning only some of these NBFRs without legislation addressing the entire group of BFRs will lead to regrettable substitution as other BFRs will enter the market again. One way out could be the application of brominated polymers, such as brominated polybutadiene-polystyrene (BrPBPS) that could serve as an alternative for HBCDD (Beach et al., 2017). However, although these are being marketed nowadays, they also have not been tested on environmental safety. It is, for example, suggested that volatile degradation products are generated when exposed to higher temperatures (Gouteux et al., 2008).

Further research on indoor environments, emission sources and potential leaching is necessary. Studies show large differences in concentrations in materials and consumer goods. This emphasizes the need for further research on emission sources. There is also an urgent need for research on the occurrence of NBFRs in materials and goods and indoor environments, as well as for toxicological studies and research on environmental fate and health effects of NBFRs.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Emma A.R. Zuiderveen: Conceptualization, Methodology, Investigation, Writing - original draft, Visualization. **J. Chris Slootweg:** Writing - review & editing. **Jacob de Boer:** Conceptualization, Writing - review & editing, Supervision.

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