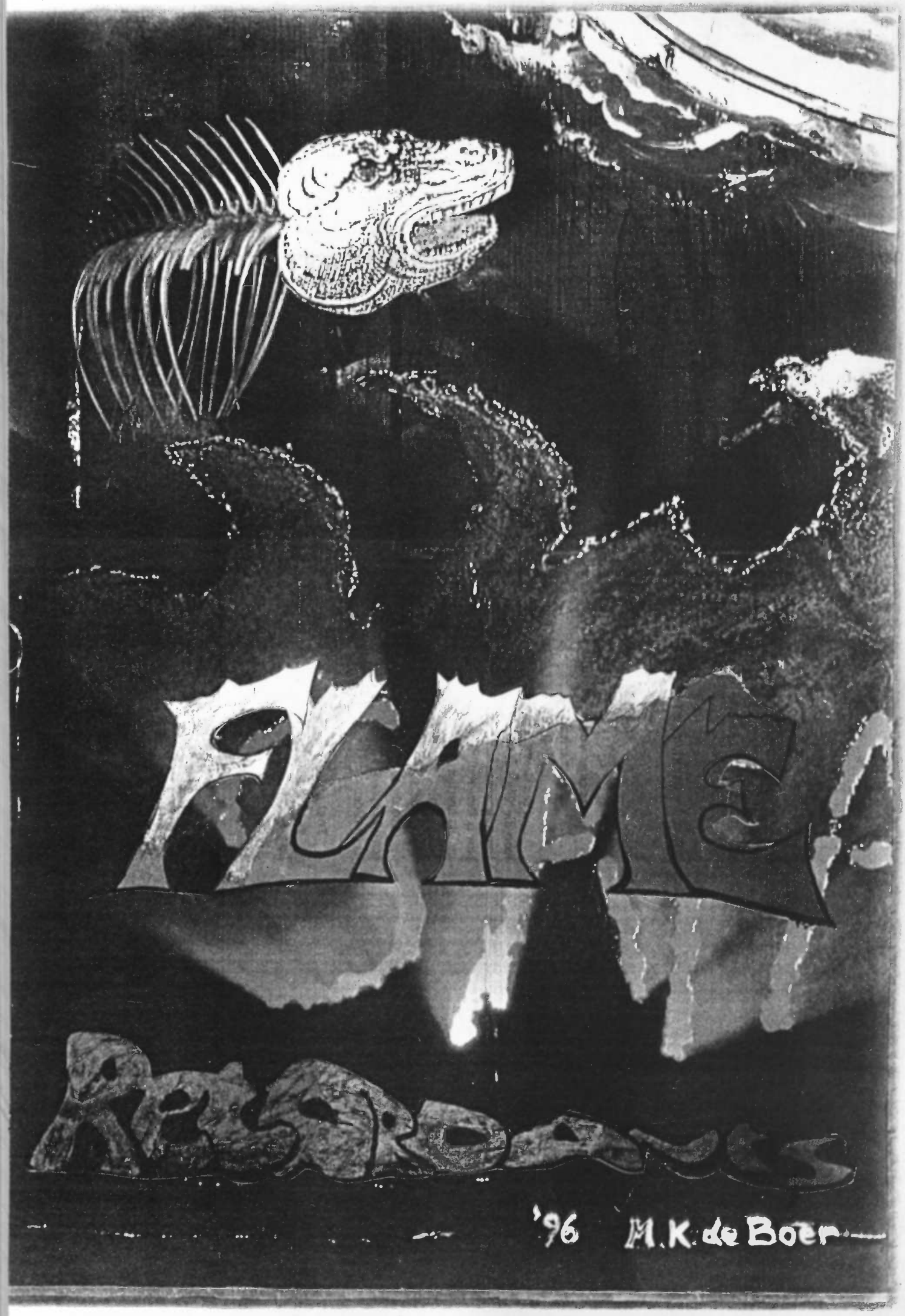
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POLYBROMINATED BIPHENYL AND DIPHENYLETHER

FLAME RETARDANTS

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ABBREVIATIONS

PBB	polybrominated biphenyl
PBDE	polybrominated diphenyl ether

DeBB	DeBDE	with 10 bromine atoms
NoBB	NoBDE	with 9 bromine atoms
OcBB	OcBDE	with 8 bromine atoms
HpBB	HpBDE	with 7 bromine atoms
HxBB	HxBDE	with 6 bromine atoms
PeBB	PeBDE	with 5 bromine atoms
TeBB	TeBDE	with 4 bromine atoms
TrBB	TrBDE	with 3 bromine atoms
DiBB	DiBDE	with 2 bromine atoms
MBB	MBDE	with 1 bromine atom

ATH	aluminium trihydrate
DDT	1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane
K_{ow}	Octanol/water partitioning coefficient
PCDD	polychlorinated dibenzodioxin
PCDF	polychlorinated dibenzofuran
PCT	polychlorinated terphenyl
PBDD	polybrominated dibenzodioxin
PBDF	polybrominated dibenzofuran
TBBPA	tetrabromobisphenol A

ECD	electron capture detector
ECNI	electron capture negative ionisation
EI	electron impact
FID	flame ionisation detection
GC	gas chromatography
HPLC	high performance liquid chromatography
HR	high resolution
MS	mass spectrometer
SIM	selected ion monetoring
UVR	ultra violet radiation

CONTENTS

SUMMARY

In this essay studies on two classes of brominated polyaromatic flame retardants are reviewed. Theoretically, 209 different congeners of both PBBs and PBDEs are possible. These congeners have specific chemical and physical properties, which lead to different biological and toxicological effects. Most studies have been based on commercial mixtures of brominated flame retardants, which complicates the pursuit of unambiguous data and insights. Only adequate quantification of individual congeners will allow comparative environmental and toxicological studies. Progress in this field depends upon the availability of pure synthesized congeners for use as standards. The present environmental levels of brominated flame retardants do not pose an immediate, major environmental risk. However, most of the PBB and PBDE congeners found in commercial flame retardants are persistent, lipophilic and bioaccumulating, which represents a definite potential threat to both human and environmental life. Therefore, prolonged commercial use of brominated flame retardants should be avoided. These compounds need to be replaced by alternative flame retardants, provided these alternatives are proven to be less harmful.

INTRODUCTION

Polybromobiphenyls (PBBs) and Polybromo diphenylethers (PBDEs) are brominated aromatic hydrocarbons, used as flame retardants. Flame retardants are chemicals that are added to polymers which are used in different materials such as electrical and electronical equipments, paint, textiles (particularly in office buildings) and in cars and aircraft to prevent them from catching fire (Sellström, 1996). PBBs are formed by substituting hydrogen by bromine in biphenyl (WHO 152, 1994). Instead of biphenyl, diphenylether is used in the bromination to PBDEs (WHO 162, 1994).
The general chemical formulas of PBB and PBDE (figure 1) show that PBB and PBDE have a large number of possible congeners, depending on the number and position of the bromine atoms on the two phenylrings. Theoretically 209 congeners of each chemical are possible. A systematic numbering system is developed by Ballschmiter and Zell (1980) for polychlorinated biphenyl (PCB) congeners which has been adopted for the corresponding PBB and PBDE congeners (Pijnenburg et al., 1995).

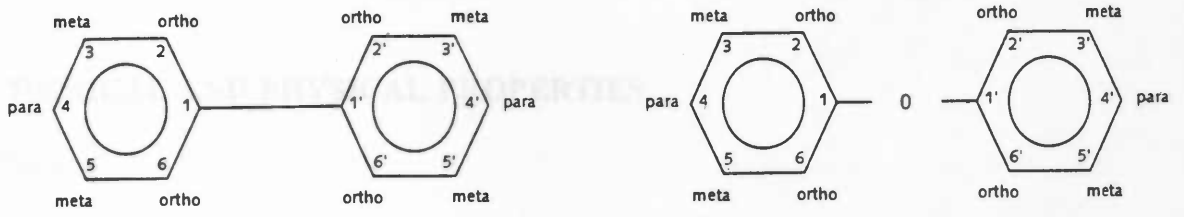

Figure 1. Basic formulas of brominated fire retardants: left; PBB right: PBDE (from Pijnenburg et al., 1995).

PBBs manufactured in early '70s for commercial use, consist mainly of hexa-, octa-, nona-, and decabromobiphenyl. They were developed as flame retardants due to their ability to meet flame resistance performance requirements, economical feasibility, and they have little effect on the flexibility of the base compounds. PBBs came to the attention of the public in 1974, when it was discovered that about 1000 pounds had been accidentally substituted for magnesium oxide as an additive in cattle feed in Michigan in 1973. After this, the production of PBBs slightly decreased (WHO 152, 1994). Still decabromobiphenyl (DeBB) and possible other PBBs are produced commercially but alternative chemicals have been introduced to replace them as flame retardants, in particular PBDEs. For PBDEs only products based on penta-, octa-, and decabromodiphenylether are of commercial interests (WHO 162,1994). The production of PBDEs increased since the end of 1970 (WHO 162, 1994).
Like other organohalogen compounds as PCBs and DDT, PBBs and PBDEs are lipophilic, and persistent (WHO 152,1994; WHO 162, 1994). The high resistance towards acids, bases, heat, light, reduction and oxidation is disadvantageous when these compounds are discharged into the environment, where they persist for a long time. Furthermore, toxic compounds, polybrominated dibenzofurans (PBDF) and dibenzodioxins (PBDD), may be formed when these flame retardants are heated (Pijnenburg et al., 1995). These physical properties of PBBs and PBDEs strongly depend upon the polymer matrix, and, when heated, upon the specific processing conditions (WHO 152, 1994; WHO 162,1994).
Chlorinated (in contradistinction to brominated) chemicals as PCB (in dielectric fluids) and

DDT (used as a pesticide) were found in high concentrations in living organisms in the late 1960s. These chemicals were shown to be hazardous to different organisms. Since then many countries have banned or restricted the use of these chemicals, and the environmental levels have decreased (Sellström, 1996). While these organochlorine compounds were banned, PBBs and PBDEs were mostly ignored. No ban has been enacted, while the production and use of brominated flame retardants increased (Shelley, 1993). Taking into account the large worldwide production and application of PBBs and PBDEs and their persistence, it is envisaged that a large part of the total production will eventually reach the environment, including the marine environment. Here, PBBs and PBDEs are likely to accumulate because of their lipophilicity and their resistance to degradative processes (Pijnenburg et al., 1995). PBDEs and PBBs are considered to be a potential threat for human health, particularly through fish consumption (de Boer and Dao 1993).
The aim of this essay is to describe chemical and physical properties, analysis, production and use, environmental fate and occurrence and the toxicity of PBB and PBDE, on the basis of an original article by Pijnenburg et al., 1995. which was actually written in 1993, supplemented with data and reports published after that article.

CHEMICAL AND PHYSICAL PROPERTIES

PBBs

PBBs are manufactured using a Friedel-Crafts type reaction in which biphenyl reacts with bromine in (or without) an organic solvent, using aluminium chloride, aluminium bromide, or iron as a catalyst (Brinkman and de Kok, 1980). During production of technical-grade DeBB (Adine 0102), biphenyl is directly brominated in a large excess of bromine, used as reactant and solvent in the presence of a Lewis acid catalyst (aluminium type). DeBB is further purified by destillating the excess bromine in the presence of a brominated solvent (WHO 152, 1994). The composition of the manufactured PBBs is given in table 1. PBBs are not known as natural products. Of the 209 possible congeners, 101 individual PBB congeners are listed in the Chemical Abstracts Service (CAS) registry at this moment (WHO 152,1994). In general, PBBs show an unusual chemical stability and resistance to acids, bases, heat, reduction and oxidation. PBBs are chemically comparable to the PCBs. However, chlorine atoms have a stronger association to polybiphenyl than bromine atoms (WHO 152, 1994). Unlike PCBs, the reactivity of PBBs has not been well studied and documented in the literature (Pomerantz et al., 1978). Like PCBs their chemical stability is dependent, in part, on the degree of bromination and the specific substitution patterns (Safe, 1984).
Some chemical and physical data of commercial PBB mixtures are given in table 2A. The chemical and physical properties depend on the PBB compound, and differs between each congener (WHO 152, 1994).
PBBs are solids with a low vapour pressure. The volatility of PBBs have a wide range and is lower than the volatility of the corresponding PCBs (Pijnenburg et al., 1995). PBBs are almost insoluble in water, and solubility decreases with increasing bromination (WHO 152, 1994). Brominated compounds have a lower solubility in water than the corresponding chlorinated compounds (Pijnenburg et al., 1995). Table 2 shows the variance in the solubility of commercial PBBs in water from different sources and qualities. Determinations of water solubility of these very hydrophobic compounds are difficult to perform, adsorption effects

on particles may influence the results. PBBs were found to be 200 times more soluble in landfill leachate than in distilled water. PBBs are soluble in various organic solvents, their solubility decreases steeply with increasing bromine content (WHO 152, 1994). Furthermore, tested PBBs have a log K_{ow} > 7, and are therefore regarded as superlipophilic compounds (Prins and Meyer, 1996).

Table 1. Composition of commercial PBB mixtures (from WHO 152, 1994).

PBB mixture (manufacturer)	Weight of bromine (%)	Weight of different homologus groups						
		Br_{10}	Br_9	Br_8	Br_7	Br_6	Br_5	Br_4
"Hexabromobiphenyl"								
FM BP-6 (Michigan Chemical)	75				13.8	62.8	10.6	2
" [Lot RP-158 (1971)]					12.5	72.5	9	4
" [Lot 6244A (1974)]					13	77.5	5	4.5
"						90	10	
"				1	18	73	8	
"					33	63	4	
"					7.7	74.5	5.6	
"					24.5	79	6	
2,2',4,4',6,6' (RFR)					12	84	1	
2,2',4,4',6,6' (Aldrich)				2	24	70	4	
"Hexabromobiphenyl" (RFR)					25 (12-25)	67 (60-80)	4 (1-11)	(2-5)[b]
Octanonabromobiphenyl								
Bromkal 80-9D (Kalk)	81-82.5	9	65	25	1			
Bromkal 80				72	27	1		
XN-1902 (Dow Chemical)[c]	82	6	47	45	2			
XN-1902 (Dow Chemical)[c]		2	34	57	7			
Lot 102-7-72 (Dow Chemical)[c]		6	60	33	1			
"Octabromobiphenyl" (RFR)		4	54	38	2			
2,2',3,3',5,5',6,6' (RFR)		1	28	46	23	2		
FR 250 13A (Dow Chemical)		8	49	31	1			
Decabromobiphenyl								
HFO 101 (Hexcel)	84	96	2					
Adine 0102 (Ugine Kuhlmann)	83-85	96	4					
Adine 0102 (Ugine Kuhlmann)		96.8	2.9	0.3				
"Decabromobiphenyl" (RFR)		71	11	7	4	4		
"DBB": Flammex B 10 (Berk)[c]		96.8	2.9	0.3				

PBDEs

Most preparation methods of PBDEs reported are patents describing the bromination of diphenylether in the presence of a catalyst (Sellström, 1996). This results in products containing mixtures of brominated diphenylethers (table 3). PBDEs have not been reported to occur naturally in the environment, but other types of brominated diphenylethers, polybrominated phenoxy phenols, have been found in marine organisms, a.o. *Dysidea herbacea*, *Dysidea chlorea*, and *Phyllospongio foliascents* (WHO 162, 1994). Vionov et al. (1991) showed that the bacteria *Vibrio sp.* associated with the sponge *Dysidea sp.* is capable of producing brominated diphenylethers.

Table 2A & B; Chemical and physical data of commercial PBB and PBDE mixtures
(from: WHO 152, 1994; WHO 162, 1994 and Pijnenburg et al.,1995)

	HxBB ($C_{12}H_4Br_6$)	OcBB ($C_{12}H_2Br_8$)	NoBB ($C_{12}H_1Br_9$)	DeBB ($C_{12}Br_{10}$)
Relative molecular mass*	627,4	785,2	864,1	943,0
Melting point (°C)	124 - 248	200 - 250	220 - 290 360 - 380 385	380 - 386
Decomposition Point (°C)	300 - 400	435	435	395 > 400
Volatility (% weight loss)		< 1% at 250 °C < 10% at 330 °C < 50% at 350 °C	1-2% at 300 °C	< 5% at 341 °C < 10% at 363 °C < 25% at 388 °C
Vapour Pressure (Pa)	25 °C; 0,000007 90 °C; 0,01 140 °C; 1 222 °C; 100			< 0,0000006 (temperature not given)
Solubility H_2O (µg/litre; 25 °C)	11 610	20-30	insoluble	< 30
destilled deionized pure BB 153	0,32 0,06 30			
good soluble in carbontetrachloride; 10 (g/kg solvent; at 28 °C)	carbontetrachloride; 300 chloroform; 400 benzene; 750 toluene; 970 dioxane; 1150	peteroleum ether; 18 benzene; 81	insoluble	
Log K_{ow}*	7,20			8,58

	TeBDE ($C_{12}H_6Br_4O$)	PeBDE ($C_{12}H_5Br_5O$)	OcBDE ($C_{12}H_2Br_8O$)	DeBDE ($C_{12}Br_{10}O$)
Relative molecular mass*	485,82	564,75	801,47	959,22
Melting point (°C)		-7 - -3 (boiling: 300)	200 79 - 89 75 - 125 170 - 220	290 - 306
Decomposition point (°C)		> 200		> 320 > 400 > 425
Volatility (% weight loss)				1% at 319 °C 5% at 353 °C 10% at 370 °C 50% at 414 °C 90% at 436 °C
Vapour Pressure (mm Hg)		22 °C: 9,3	25 °C < 10^{-7}	20 °C < 10^{-6} 250 °C < 1 278 °C; 2,03 306 °C; 5,03
Solubility H_2O (at 25 °C)		9 x 10^{-7} mg/litre at 20 °C	< 1 g/litre	20 - 30 µg/litre
good soluble in (g/kg solvent; at 25 °C)		methanol; 10 (and other organic solvents)	toluene; 190 (353) benzene; 200 styrene: 250	o-xylene: 8,7
Log K_{ow}*	5,87 - 6,16	6,64 - 6,97	8,35 - 8,90	9,97

* means data of BB or BDE congener

Table 3. Composition of commercial PBDEs (from WHO 162, 1994).

Product	Composition								
	PBDE[a]	TrBDE	TeBDE	PeBDE	HxBDE	HpBDE	OBDE	NBDE	DeBDE
DeBDE								0.3-3%	97-98%
OBDE					10-12%	43-44%	31-35%	9-11%	0-1%
PeBDE		0-1%	24-38%	50-62%	4-8%				
TeBDE[b]	7.6%	-	41-41.7%	44.4-45%	6-7%				

[a]Unknown structure.
[b]No longer commercially produced. Analysis of one single sample.

Because of the presence of an oxygen atom, there is less similarity in molecular structure between PBDEs and PCBs than between PBBs and PCBs (WHO 162, 1994). The commercial PBDEs are rather stable compounds with boiling points ranging between 310 and 425 °C (WHO 162, 1994), and with low vapour pressures (table 2B) (WHO 162, 1994; Sellström, 1996). The volatility of PBDEs is low and their solubility in water is very low, especially that of higher brominated diphenylethers. It was concluded that higher brominated compounds are more persistent than lower brominated compounds. PBDEs are soluble in organic solvents. The commercial PBDEs are lipophilic substances of which the log K_{ow} increases with increasing bromine content (WHO 162, 1994).

ANALYSIS

PBBs

Analytical methods for the determination of PBBs were adapted from established methods for chlorinated hydrocarbon insecticides (like DDT) and PCBs (WHO 152, 1994). Usually hexane is used as solvent in the analysis of PBB mixtures and individual congeners.
Griffin and Chov (1981) found that for the extraction of PBBs from soils and sediments the use of a polar organic solvent was important. The best results were obtained with hexane/acetone (9:1). Extraction was followed by further sample-clean up with Florisil.
Fehringer (1975) describes the use of dichloromethane for extraction of PBBs from dry animal food. Sample-clean up is performed with Florisil columns.
Extraction of blood and serum follows pretreatment of the serum with methanol, and extraction is performed with a hexane/ether mixture. This method described by Burse et al. (1980) is a standard extraction method for blood and serum, and has been used in most studies. Florisil columns are used in the sample-clean up. An analytical method was developed to quantitate PCBs and PBBs in human serum. This method includes a hexane-ethyl ether extraction of methanol-denatured serum, and an adsorption chromatography with deactivated silica gel (Needham, 1981).
Since PBBs are readily soluble in fat, the extraction of PBBs from adipose and other tissues is more complex. They can be co-extracted together with the fat from the tissue sample but afterwards, an intensive clean up procedure for PBBs is necessary. Various sample clean up methods such as adsorption chromatography with Florisil, gel permeation chromatography, Florisil cartridges and Unitrex have been proposed (WHO 152, 1994).
For analysis of PBBs in biological samples from marine or freshwater environment, similar extraction and clean up techniques as for PCBs are used. Lipids can be removed from

extracted samples by use of gel permeation techniques or hydrolysis. Usually PBBs and PCBs are separated from more polar compounds by adsorption chromatography on silica gel or Florisil. Isolation of coplanar compounds from the major compounds in the extract is achieved by using activated charcoal, since this adsorbs the planar molecules more strongly than the non-planar ones. Brominated naphthalenes, dioxins and furans, will also be separated from the non-planar compounds in these steps. To aid these separations, high performance liquid chromatography (HPLC) methods are now being adopted (WHO 152, 1994). Soxhlet extraction with dichloromethane/*n*-pentane, followed by clean up over alumina columns and fractionation over silicagel columns, results in recoveries over 95% for all PBBs. Saponification may be an alternative, but decomposition of some PBB congeners may occur as in the case of PCBs (Pijnenburg et al., 1995).
Recovery of PBBs using established methods is in the range of 80-90% (Fries, 1985). The solvent system used for sample extraction can affect recovery, the optimal solvent condition depending on the nature of the biological sample (WHO 152, 1994).
Furthermore PBBs adsorb to glass more tenaciously than other halogenated hydrocarbons, and are not easy to remove by the usual cleaning methods. Using disposable glassware prevents erroneous values in the data (Willet et al., 1978).
The 209 possible PBB congeners have a wide range of volatility, which causes complex separation problems. Oven temperatures vary between 240°C and 300°C. Although most PBBs elute after PCBs, higher chlorinated PCBs may interfere with lower brominated PBBs (Pijnenburg et al., 1995). Decachlorobiphenyl caused most interference in the analytical method for quantification of PBBs in human serum (Needham, 1981). Polychlorinated terphenyls (PCTs) may also interfere with PBBs (Wester et al., 1995). Therefore mass spectrometry (MS) is the most advantageous technique for detection of peaks after separation (Pijnenburg et al., 1995). Quantification can be achieved by comparison with known standards (WHO 152, 1994). In PBB detection commercial mixtures are used, since the commercial availability of pure congener standards is limited. The synthesis of pure congeners for use as standards is a prerequisite for advances in chemical analysis, as well as research into toxicological and biological effects of PBBs (WHO 152,1994). Although some individual PBB congeners are available as standards, there is only one study reported. This study described the use of 2-BB and 4-BB as standards. These standards were purchased from Acru Standard, Inc (New Haven,CT) in neat form and were dissolved in ethyl alcohol. The chemicals were 99% pure as determined by GC and FID (Kholkute et al., 1994). Unclear was whether 2-BB and 4-BB are MBBs or DiBB and TeBB, since the authors consequently referred to these compounds as 'PBB's, illustrating the necessity of using proper systematical names when reporting such studies. Some routes for synthesizing of PBB congeners have been described by Sundström et al. (1976 b), Robertson et al. (1980, 1982 a, 1984 a), Höfler et al. (1988) and Kubizak et al. (1989).
A recent method of detection is electron capture negative ionisation (ECNI) as ionization technique in combination with GC-MS analysis. This method is advantageous because it offers a high sensitivity for compounds with four or more bromine atoms (de Boer, 1995). The sensitivity of ECNI for these compounds is approximately 10 times higher than with the use of an electron capture detector (ECD) (Pijnenburg et al., 1995). In the analytical method which was developed to quantitate PCBs and PBBs in human serum, GC is used with an ECD (Needham, 1981). Because the response, and therefore the sensitivity, of the ECD depends on the position of the halogen on the biphenyl nucleus as well as the number of halogen atoms, it is necessary to run a standard for each compound to be determined (WHO 152, 1994). The use of narrow bore (0,15 mm i.d.) capillary columns is advised to obtain the required

resolution (Pijnenburg et al., 1995).
Because of its low specificity and sensitivity flame ionisation detection (FID) can only be used in the analysis of standard substances (Krüger, 1988). The same limited application is envisaged for the method with the microwave-induced plasma emission detector, which is not sensitive enough for environmental samples (WHO 152, 1994).

PBDEs

Extraction and clean-up techniques for the analysis of PBDE residues in biological samples are similar to those developed for PBB. Table 4 shows several methods to determine PBDEs in various media. Most methods are based on extraction with organic solvents, purification of the extracts by gel permeation or adsorption chromatography, and determination mainly by GC, either with ECD or coupled with MS, with electron impact (EI) or NCI. The recovery for the different PBDEs is generally higher than 80% (WHO 162, 1994).

Table 4. Analytical methods for PBDE (from WHO 162, 1994).

Sample	Extraction and clean-up	Separation and detection	Limit of determination	Reference
Sewage	extract with chloroform; evaporate and dissolve residue in ethanol	GC/MS	0.06 mg/kg	Kaart & Kokk (1987)
Sediment	extract with acetone; clean-up on Florisil	NAA; GC/EC	< 5 µg/kg < 5 µg/kg	Watanabe et al. (1987b)
Fish	extract with acetone-hexane + hexane-ethyl ether; treatment with sulfuric acid or clean-up on alumina; chromatography on silica gel	GC/EC; GC/MS	limit of detection 0.1 mg/kg fat	Andersson & Blomkvist (1981)
Animal tissues (Multi-residue method)	homogenize; extract with *n*-hexane-acetone; treatment with sulfuric acid; gel permeation chromatography; chromatography or silica gel; chromatography or activated charcoal	GC/MS (NCI)	10 ng/kg	Jansson et al. (1991)
Rat liver	extract with tetrahydrofuran	HPLC		Rogers & Hill (1980)
Fish	extract freeze-dried powdered sample with pet. ether; gel permeation chromatography; clean-up on Florisil; elute with hexane	GC/MS (NCI/SIM)	< 5 µg/kg fat	Krüger (1988)
Cow's milk	centrifuge; gel permeation chromatography; clean-up on Florisil; elute with hexane	GC/MS (NCI/SIM)	< 2.5 µg/kg fat	Krüger (1988)
Human milk	extract with potassium oxalate/ethanol/diethyl ether/pentane; gel permeation chromatography; clean-up on Florisil; elute with hexane	GC/MS (NCI/SIM)	< 0.6 µg/kg fat	Krüger (1988)
Human adipose tissue	extract with methylene chloride; evaporate; clean-up on silica gel followed by clean-up on alumina and on a carbon/silica gel column	HRGC/HRMS[a]	limit of detection 0.73-120 ng/kg (different congeners)	Cramer et al. (1990a,b)
Commercial PBDE	homogenize and dissolve in tetrachloromethane for HPLC and GC/MS or *n*-hexane for TLC/UV	HPLC; GC/MS; TLC/UV	-	deKok et al. (1979)

[a]High resolution gas chromatography/high resolution mass spectrometry.

Other extraction methods described for PBDEs in the literature are basically batch and Soxhlet extractions. The clean up methods for biological, sediment, and sewage sludge samples are different to the same extent, depending on other compounds of interest (Sellström, 1996).
A multi-residue method has also been developed by Jansson et al. (1991). This method includes a multi-step separation enabling the determination of several polychlorinated an polybrominated pollutants in biological samples (WHO 162, 1994). However, the recovery of 2,2',4,4'-TeBDE with this method is only 49% (Pijnenburg et al., 1995).
The extraction of DeBDE (and also DeBB) proves more difficult than other PBDEs, but a good solvent system is hexane/acetate (3:1)(pers. comm. Sellström, 1996).
Another analytical method was used for the *in vitro* biotransformation of PBDEs (particularly DeBDE) in microsomal preparations of livers of marine mammals and birds. The method for extracting PBDE from the incubation mixture was most efficient using hexane/methanol (8:1), followed by a clean up with concentrated sulphuric acid and separation using a semi wide bore column in the gas chromatography analysis (Greve et al., 1996).
Typical GC analysis is performed using a nonpolar capillary column (15-60 m) of methyltype (SE-30, OV-1, OV-101) or methyl + 5% phenyl groups (DB-5,SE-54,CP-SIL8CB) (Sellström, 1996).
Both GC-ECD and GC-MS with EI or ECNI may be used for the final analysis of PBDEs (Pijnenburg et al, 1995). ECNI-MS is a very sensitive method for many halogenated compounds (Sellström). Using GC-MS, the type of reaction gas can influence the data. A study of PBDE residues in guillemot eggs showed an increase in levels of 2,2',4,4'-TeBDE, an unidentified PeBDE, and 2,2',4,4',5-PeBDE of respectively 10-35%, 25-80%, and 0-20% after re-analysis using ammonia as reaction gas instead of methane (Sellström 1996).
Another variety of the GC-MS detection method is high resolution GC/ high resolution MS (HRGC-HRMS). Not only human adipose tissue (table 4) can be analysed with HRGC-HRMS. Studies are described by Loganathan et al. (1995), and Takasuga et al. (1995), investigating analysis of PBDE residues in environmental samples with HRGC-HRMS. After the standard clean up a further carbon clean up stage with HPLC porous graphitic carbon was added. The mass spectrometer was operated in standard peak top selected ion monitoring (SIM) mode after GC-MS. Additionally mass peak profile monitoring acquisition at high resolution and low resolution scanning were performed to identify the interferences. With this method the identification of PBDEs as interferences to heptachlorinated dibenzofurans in the analysis of routine environmental samples can be quantified (Takasuga et al., 1995).
In most studies the technical mixture Bromkal 70-5 DE is used as external standard. The percentage of PBDE congeners of Bromkal 70-5 DE is 44% 2,2',4,4'-TeBDE, 48% 2,2',4,4',5-PeBDE an 8% of an unknown PeBDE (de Boer and Dao, 1993; Pijnenburg et al., 1995; Sellström, 1996). Like PBB analysis, the analysis of PBDEs requires individual PBDE congeners as analytical standards. Synthesized pure standards of 2,2',4,4'-TeBDE, 2,2',4,4',5-PeBDE and 2,2',4,4',5,5'-HxBDE (de Boer and Dao, 1993; Sellström, 1996) are available. Sellström (1996) has the opinion that the three congeners so far cannot replace the Bromkal mixture as standard, because no single congener of the unknown PeBDE has been available. Comparison of the Bromkal standard used with the 2,2',4,4'-TeBDE, 2,2',4,4',5-PeBDE standards showed that the percentage of the TeBDE in this mixture was 36,1% and PeBDE 35,5% (de Boer & Dao 1993). De Boer and Dao (1993) made a correction of the initial estimation of -5,6% for 2,2',4,4'-TeBDE and -8,9 % for 2,2',4,4',5-PeBDE in their overview of BDE data in aquatic biota and sediments. At present, samples are quantified with Bromkal 70-5 DE and a mixture of three congeners (2,2',4,4'-TeBDE, 2,2',4,4',5-PeBDE and 2,2',4,4',5,5'-HxBDE), but the results are not yet fully evaluated for monitoring purposes

(Sellström, 1996).
A study describing the uptake of DeBDE in rainbow trout shows that more standards are available: 2,2',3,4,4'-PeBDE, DeBDE and, an unidentified PeBDE (Kierkegaard et al. 1995). Most of the pure standards were synthesized by Å. Bergman, Stockholm University (Sellström, 1996; De Boer and Dao, 1993). Wolf and Rimkus (1985) described the synthesis of 2,2',4,4'-TeBDE for the analysis of this congener in fish.

PRODUCTION

PBBs and PBDEs belong to the group of brominated organic compounds used as flame retardants. Flame retardants are valued for their ability to inhibit combustion in plastics, textiles, electric, and other materials. There are different groups of flame retardants: inorganic and organic chemicals. Usually they are divided into reactive and additive flame retardants.
Reactive flame retardants have the same functional groups as the monomer with which they react. They are covalently bound to the polymer and are therefore less likely to leach to the environment. Reactive type flame retardants offer advantages such as polymer strength permanency and solvent resistance. Disadvantageous is that they are polymer specific (Hairston, 1995).
Additive flame retardants are not chemically incorporated into the polymer molecule. The additives are only mixed with or dissolved in the material and can therefore migrate out of the product during its entire lifetime (Sellström, 1996).
What all flame retardants have in common is that they start to decompose when heated. A critical factor in the choice of a flame retardant is therefore its thermal stability with respect to that of the polymer. The ideal situation is when the flame retardant decomposes at about 50% below the combustion temperature of the polymer. This is the case with most organic bromine compounds and most synthetic polymers (Sellström, 1996). Furthermore brominated flame retardants are economically feasible, and they have little effect on the flexibility of the base compounds (Mumma and Wallace, 1975). Because of the advantages mentioned above, the industrial use of brominated compounds is attractive.

PBBs

The commercial used PBB mixtures consist mainly of HxBB, OcBB, NoBB, and DeBB (table 1). Commercially manufactured PBBs are primarily processed as flame retardant. Further potential uses of PBBs are: in the synthesis of biphenylesters or in a modified Wirtz-Fittig synthesis; in light sensitive compositions to act as colour activators; as relative molecular mass control agents for polybutadiene; as wood preservatives; as voltage stabilizing agents in electrical insulation; as functional fluids, such as diëlectric media (Neufeld et al., 1977).
In the early 1970s PBBs were introduced as flame retardants. In the USA the production of HxBB ceased as a result of the Michigan disaster (table 5). OcBB and DeBB were produced until 1979 (WHO 152, 1994). There was no import of any PBB mixtures. Since 1975-1976 all PBBs manufactured in the USA have been exported, mainly to Europe (Brinkman and de Kok, 1980). In Japan some PBBs were imported upto 1978, but there was no production. A mixture of highly brominated PBBs (Bromkal 80-9D) was produced in Germany until mid 1985 (WHO 152, 1994). The production of DeBB in Great Britain was discontinued in 1977 (Neufeld et al., 1977). A French firm is currently producing technically grade DeBB (Adine

0102) in quantities of a few hundred thousand kg/year. It is marketed in France, Great Brittain, Spain and the Netherlands (Atochem, 1990). In the Netherlands more than 200 tonnes DeBB/year (1989) were used (UBA, 1989). An Israelic company with two bromine plants in the Netherlands denied the production of PBBs (Neufeld et al., 1977).

Table 5. Commercial production of PBBs in the USA, 1970-1976 (from Di Carlo et al., 1978).

	Estimated production in thousand kg							
Product	1970	1971	1972	1973	1974	1975	1976	1970-76
Hexabromobiphenyl	9.5	84.2	1011	1770	2221	0	0	5369
Octabromobiphenyl and decabromobiphenyl	14.1	14.1	14.6	163	48	77.3	366	702
Total PBBs	23.6	98.3	1025	1933	2269	77.3	366	6071

Most research of PBBs has been carried out on Fire Master BP-6 and FF-1, which were involved in the Michigan disaster. The PBB composition of Fire Master changes from batch to batch (table 1), but also mixed bromochlorobiphenyls and polybrominated naphthalenes have been observed as minor components (WHO 152, 1994). Approximately 20 compounds other than PBBs were tentatively identified in Fire Master (Hass et al.,1978). An extensive study was performed on a large number of batches of Fire Master, analysed for the toxic compounds PBDD and PBDF. These compounds were found in only one sample of Adine 0102 (WHO 152, 1994).

PBDEs

Products based on penta-, octa-,and decaBDE are of commercial interests (table 3). PBDEs are mainly used as a flame retardant. There are eight manufacturers who currently produce PBDEs. They are:

Dead Sea Bromines and Eurobrome	the Netherlands
Atochem	France
Great Lakes Chemical Ltd	Great Britain
Great Lakes Chemical Corporation	USA
Ethyl Corporation	USA
Tosoh	Japan
Matsunaga	Japan
Nippo	Japan

The global production of DeBDE is approximately 30.000 tonnes/year. The total annual consumption of PBDEs is 40.000 tonnes (WHO 162, 1994; Sellström, 1996).

CONSUMPTION

Due to more stringent fire regulations in many countries and the increased use of plastic materials and synthetic fibres, the use of flame retardants has increased. In 1992, 600.000 tonnes of flame retardants were used worldwide, 150.000 tonnes were brominated compounds. 50.000 Tonnes of these were the reactive flame retardant with TBBPA and its derivatives and 40.000 tonnes were PBDEs (Sellström, 1996).
The annual global consumption of PBDE is 40.000 tonnes (30.000 tonnes DeBDE, 6000 tonnes OcBDE and 4000 tonnes PeBDE) (WHO 162,1994; Sellström, 1996). Data on the usage of PBDE are (from WHO 162, 1994):

Germany	3000 - 5000 tonnes/year (1991)
Sweden	1400 - 2000 tonnes/year (1991)
	400 tonnes/year (1991, from Sellström, 1996)
the Netherlands	3300 - 3700 tonnes/year (1992)
Great Britain	2000 tonnes/year (1993)

The annual consumption of flame retardants in Japan is shown in figure 2. Here there was no usage of TeBDEs after 1990. Inorganic flame retardants (a.o.ATH) were mainly used, but there is an increase in the use of brominated organic flame retardants (Sellström, 1996).

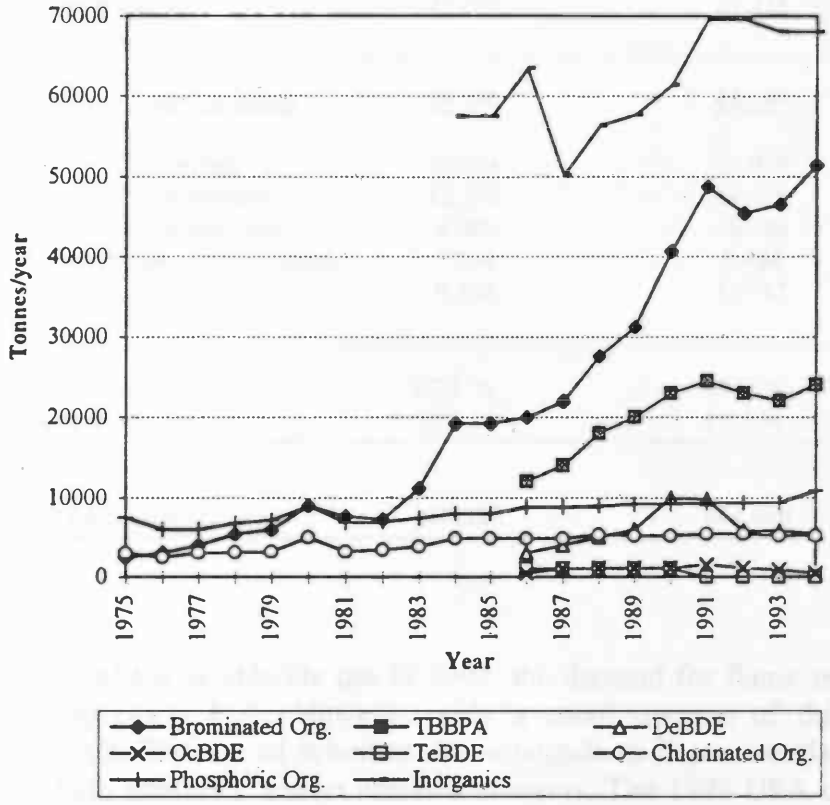

Figure 2. Trends in consumption of flame retardants in Japan (from Sellström, 1996).

In the USA brominated flame retardants belong to the most widely used additive flame retardants (table 6). Expected is that in the USA the demand for additive products will increase about 5,3%/year, to 476.700 tonnes in 1998. Despite their specificity, the demand for reactive products is expected to increase 4,6 %/year to 68.100 tonnes in 1998, as new products are introduced into the market. Expected is that the brominated flame retardants consumption will increase upto 50.848 tonnes in the USA (Hairston, 1995).

Table 6. The flame retardant demand in 1993 and the expected flame retardant demand of 1998 in the USA, in tonnes (from Hairston, 1995).

Product	1993	1998
Additive flame retardant	367.740	476.700
Aluminatrihydrate	196.128	256.510
Phosphorus compounds	44.038	57.658
Bromine compounds	39.952	50.848
Antimony oxide	28.148	35.412
Chlorinated compounds	24.970	29.964
Boron compounds	7.264	9.080
other additives	27.240	37.228
Reactive flame retardant	54.480	68.100
Epoxy intermediates	16.344	19.976
Polyester intermediates	12.258	14.528
Urethane intermediates	9.080	10.896
Polycarbonate intermediates	7.264	9.988
other intermediates	9.534	12.712
Percent Additive	87,1 %	87,5 %
Percent Reactive	12,9 %	12,5 %
TOTAL Demand	**422.220**	**544.800**

Compared with data of the worldwide use in 1992, the demand for flame retardants in the USA in 1993 is extremely high. However, only a small fraction of this consisted of brominated compounds. The use of brominated compounds as flame retardants in Japan in 1993 was higher, both relatively and in absolute amounts. The 1998 USA consumption of brominated compounds (in absolute amounts) is expected to reach the same level as Japan in 1994. Unfortunately more accurate data on flame retardants demands in Europe are available. The European consumption of brominated compounds is estimated to be at a similar level as in Japan and the USA.

COMBUSTION AND RECYCLING OF PBBs AND PBDEs

The persistence of brominated flame retardants is advantageous to the industry, but a disadvantage to the environment. Another disadvantage of brominated flame retardants is that PBDDs and PBDFs may be formed during combustion. There are hundreds of possible congeners of halogenated dibenzodioxins and dibenzofurans. However, only congeners with substituents in the 2,3,7,8-positions are of toxicological significance. In many reports, only the total levels of PBDF and PBDD are given without regard to substitution pattern; such totals are of limited value in the estimation of possible risks (WHO 162, 1994). Nevertheless, little is known about the toxicity of brominated and brominated/chlorinated dioxins and furans. They are estimated to be in the same order as those of PCDD and PCDF (WHO 152, 1994; WHO 162, 1994).

Debromination reactions of higher brominated flame retardants lead to lower brominated PBDF and PBDD congeners (WHO 162, 1994). On pyrolysis PBDEs produce larger amounts of dioxins and furans than PBBs, and in this respect PBDEs are more toxic than PBBs. Most likely is that with the oxidation of PBDE, PBDFs and PBDDs are formed in intramolecular cyclyzation reactions involving the attack by oxygen on the diphenylether system (figure 3) (Bieniek et al., 1989). Most of the reports have indicated that maximum production of PBDFs and/or PBDDs were observed at temperatures of 400 - 800 °C, depending on the type of brominated flame retardant, and that the 2,3,7,8 substituted compounds were seen only in very low concentrations (WHO 162, 1994). At 600 °C 2,3,7,8-TeBDD and TeBDF in concentrations of 0,01 - 7 ppm and 0,01 - 6 ppm respectively, are formed from plastics containing DeBDE or PBDE as flame retardant. With increasing temperature the concentration of these isomers decreases until they are no longer detectable above 800 °C (detection limit 0,01 ppm) (Lahaniatis et al., 1991).

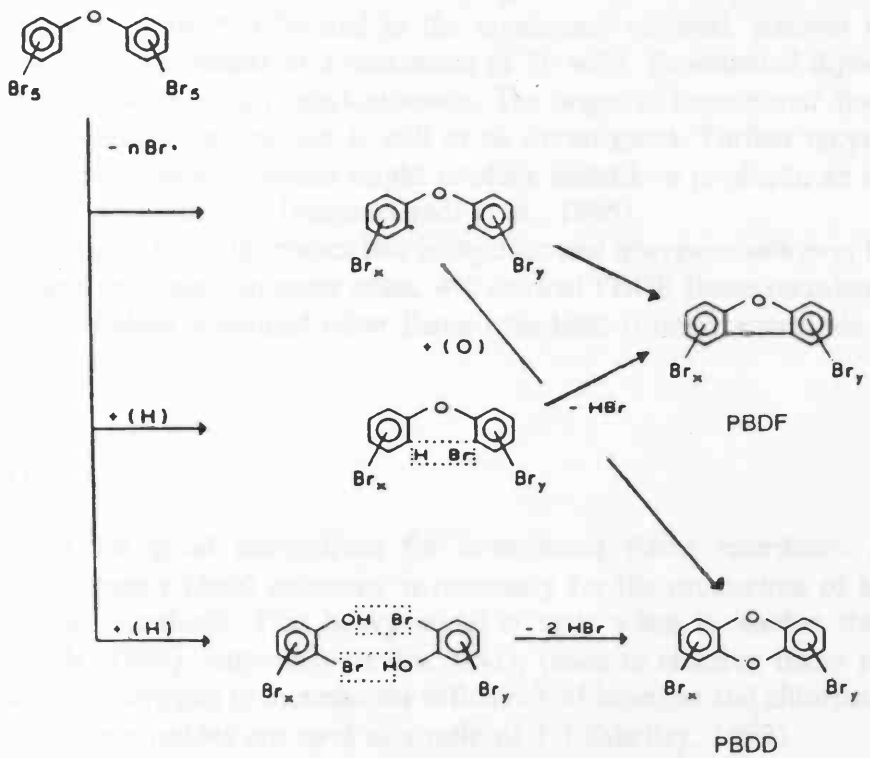

Figure 3. Possible mechanisms for the formation of PBDFs and PBDDs from DeBDE (from Bieniek et al., 1989).

The results of laboratory pyrolysis experiments with PBDE and PBB, showed that PBDF and/or PBDD were formed in various concentrations, depending on the type of PBDE and PBB, the polymer matrix, the specific processing conditions (temperature, presence of oxygen, etc.) and equipment used, and the presence of Sb_2O_3. This antimony oxide, used as synergyst in flame retardants, plays a catalytic role in the formation of PBDF and PBDD. Because the behaviour of PBDE is strongly dependent upon the polymer matrix and upon the specific processing conditions, laboratory pyrolysis experiments can hardly be used as reliable models to predict behaviour in commercial moulding operations (WHO 162, 1994).
As with PCB disposal, the destruction of PBB- and PBDE-contaminated waste should be carefully controlled. For PCBs, a burning temperature above 1000 °C for 2 seconds is recommended (WHO/EURO, 1987). Since PBDEs and PBBs are undetectable above 800 °C, the same approach might be effective for PBDE and PBB (WHO 152, 1994).
An overwhelming body of toxicology studies has shown that in a fire situation, the toxicity and volume of carbon monoxide overshadows the toxicity of brominated offgasses (which are often produced in ppb range), so their significance remains subject to debate. So far no ban has been enacted in Europe or the USA (Shelley, 1993). European electronics manufacturers state that they banned PBDEs as additives for flame retardants in the mid eighties (Dumler-Gradl et al., 1995).
Another objection against flame retardants is that recycling of plastics proves difficult, because of the content of the additives PBB and PBDE (Consumentengids, 1995; Dumler-Gradl et al., 1995). In order to evaluate electronic devices as a source for dioxins, electronics and recycled materials of obsolete electronics were subjected to detailed analytical investigations. The results prove that PBDEs are still present as additives in plastics although they were banned by European electronics manufacturers. Pyrolysis of flame retardant material of printed circuit board and electronics components (laboratory scale) produces high amounts of brominated dioxins and furans (2,3,7,8-TeBDF, 28860 ng/kg: residue after quarts flask pyrolysis in N_2/H_2atomosphere at 1100 °C) located in the condensed material. Known was that these plastics contain flame retardants to a maximum of 20 wt%. Brominated diphenylethers can be extracted from plastics using propylcarbonate. The origin of brominated dioxin and furans detectable in propylcarbonate extract is still to be investigated. Further recycling activities which process flame retarded plastics might produce hazardous products, an aspect that has to be investigated more closely (Dumler-Gradl et al., 1995).
Investigation of hundreds of electronics like computers and television sets over the last 4 years showed PBB flame retardants in some cases. 4% showed PBDE flame retardants. In total 1/6 of the electronics studied contained other flame retardants (Consumentengids, 1995).

ALTERNATIVES

There is a need for good alternatives for brominated flame retardants. Besides other disadvantages, the heavy metal antimony is necessary for the production of brominated (or chlorinated) flame retardants. This heavy metal is toxic when it reaches the environment (Consumentengids, 1995). Antimony oxides, Sb_2O_5 (used in reactive flame retardants) and Sb_2O_3, are used as synergysts to increase the efficiency of bromine and chlorine. Bromine and chlorine and antimony oxides are used at a ratio of 1:3 (Shelley, 1993).
Non-halogenated products, based mainly on phosphorus, aluminium trihydrate (ATH) and magnesiumhydroxide ($Mg(OH)_2$), halt flame spread without the formation of halogenated

byproducts. However, at relatively high loading they can compromise the polymer's mechanical properties (Shelley, 1993). The additive flame retardant ATH is multifunctional, cheap, and widely used as a filler and plasticizer. It is particularly used in large quantities in carpet underlay (Hairston, 1995). Despite high loadings requirements (20 - 70 wt.%) these inorganics are widely used because of their ability to suppress smoke generation and avoid the production of toxic offgasses (Shelley, 1993).
Consumption of halogenated additives is expected to decline as the market moves towards synergistic systems that mix flame retardants such as antimony oxide, phosphorus, and zinc borate with a halogen (Hairston, 1995).
To combine fire resistance with low smoke and gas formation, a low halogen flame retardant is produced, which contains just 25-26% bromine, which is used at loadings of 4-6%. Most of the widely used halogenated compounds contain up to 80% halogen (Shelley, 1993).
The so-called intumescents is another class of flame retardants. It is a low smoke release flame retardant which combine nitrogen and phosphorus. They are more costly than many halogenated compounds but are used in a.o. wire-and-cable and electronic housing uses where toxic smoke poses an immediate threat (Shelley, 1993).
Because reactive type flame retardants are polymer-specific their application is limited. There are several reactive flame retardants, specifically produced and all different in composition. For example, there is a 25% pelletized concentrate of antimony pentoxide, bromine and polypropylene resin of various melt flow indices, which is geared to PP fibers for textiles and carpets, and also to PP thin-film applications where colour and clarity are desired. Furthermore dibromostyrene (DBS), a reactive styrene monomer, is used to make copolymers for adhesives and coatings. DBS can also be used to impart flame retardancy in polyolefins (Hairston, 1995).
For structural applications there is a line of glass yarn fabrics engineered. Woven with Advantex glass yarn it can withstand high temperatures. The silica based fabrics are inert and there is nothing to be offgassed. A new product is composed of two different forms of glass fiber, the material is fire, smoke and flame resistant, without flame retardants (Hairston, 1995).

EMISSION, DISTRIBUTION, AND TRANSFORMATION OF PBBs AND PBDEs IN THE ENVIRONMENT

Losses of PBBs and PBDEs into the environment during normal production can occur through emission into the air, waste waters, losses into the soil, and to landfills. These chemicals can also enter the environment during shipping and handling, and accidentally, as occurred in Michigan with PBBs, in cattlefeed. There is also a possibility of their entrance into the environment as a result of the incineration of materials containing PBBs and PBDEs as well as during accidental fires, together with the formation of other toxic chemicals, as such, or as degradation products (WHO 152, 1994; WHO 162, 1994).
Both PBBs and PBDEs are persistent, lipophilic, and only slightly soluble in water. Lipophilic chemicals have the inclination to concentrate at non-polar surfaces of particles, and in living organisms. Strong lipophilic compounds prefer solid particles in soil or sediments. So, the hydrophobic properties of PBBs and PBDEs make them to be easily adsorbed from aqueous solutions onto soil (WHO 152, 1994; WHO 162, 1994). Preferential adsorption of PBB congeners was noted, depending on the characteristics of the soil (e.g. organic content) and

the degree and position of bromine substitution (WHO 152, 1994). Once introduced into the soil PBBs and PBDEs do not appear to be translocated readily. The solubility of PBBs and PBDEs in water decreases with increasing bromination, so congeners with low bromine content are more easily distributed in the aquatic environment (WHO 152, 1994; WHO 162, 1994). The principal known routes of PBBs into the aquatic environment are from industrial waste discharge and leachate from dumping sites into receiving waters and from erosion of polluted soils. Pollution of soils can originate from point sources, such as PBB plant areas and waste dumps (WHO 152, 1994; WHO 162, 1994).

Both PBBs and PBDEs are slowly degraded in the environment. Fifteen years after the Michigan disaster (1988) cores of the Pine River sediments contained 10 -12% non-Fire Master compounds indicating a partial degradation of the PBB residues in the soil. It appeared that bromines were selectively removed from the *meta*- and *para*-positions. Micro-organisms isolated from Pine Rivers sediment were capable of debrominating Fire Master PBB compounds (Pijnenburg et al., 1995). Organic co-contaminants like petroleum products and heavy metals inhibited *in situ* debromination in the most contaminated Pine River sediment (Morris et al., 1993). Microbial degradation of PCBs occurs by anaerobic dechlorination followed by aerobic ring fission (figure 4, Prins and Meyer, 1996). Since the physical and chemical properties of PBBs resembles those of PCBs (more than PBDEs) the same microbial degradation could be possible for PBBs and, perhaps also for PBDEs. Anaerobic micro-organisms eluted form PCB-contaminated river sediments were shown to reductive debrominate a Fire Master mixture. Two bacterial strains of the genus *Pseudomonas* isolated from a lake sediment, using *p*-chlorobiphenyl as a sole carbon source , were capable of degrading 2- and 4-bromobiphenyl, but unable to degrade 4,4' dibromobiphenyl (WHO 152, 1994).

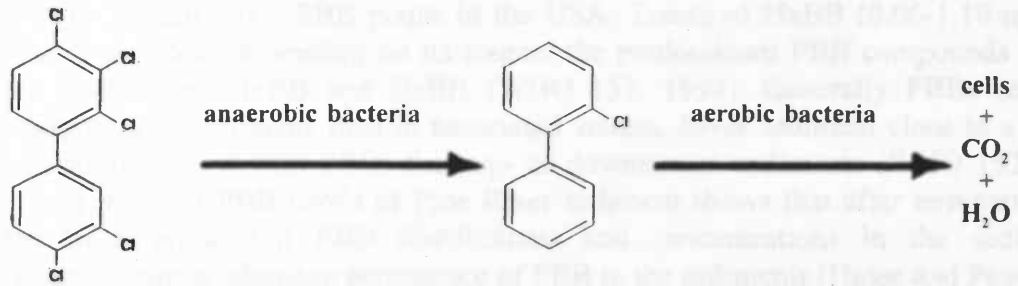

Figure 4. Microbial degradation of PCB (from Prins and Meyer, 1996).

Degradation of PBBs by purely abiotic chemical reactions, excluding photochemical reactions (photodegradation), is considered an unlikely environmental sink (WHO 152, 1994).
Earlier studies on photodegradation using lower brominated PBB congeners (TeBB and lower), reported a preferential loss of *ortho* bromines (Bunce et al., 1975; Ruzo et al., 1976). On photolysis of Fire Master BP-6 (solvent cyclohexane), no preferential loss of *ortho* bromines was found but other congeners, known as relatively toxic (e.g. 2,3',4,4',5' PeBB) were enriched (Robertson et al., 1983). The main component of Fire Master BP-6; 2,2',4,4',5,5' HxBB (BB 153) was consistently found in relatively high levels, and degradation of this compound occurred more rapid than with its hexachloro analogue. Furthermore PBBs degraded readily by UVR under laboratory conditions (WHO 152, 1994). Watanabe et al. (1986) reported that DeBDE dissolved in hexane can be degraded to NoBDE, OcBDE, HpBDE and HxBDE.

Studies have been performed on the photodegradation of DeBDE in organic solvents and water. DeBDE was irradiated in hexane solution with ultra violet radiation (UVR) and sunlight (WHO 162, 1994). A mixture of tri- to octaBDE congeners was detected. Furthermore a large number of PBDFs containing 1-6 bromoatoms and small amounts of polybromobenzenes were formed. Photodegradation of PBDE in water does not lead to the formation of lower BDE or BDF, but little is known about photodegradation in other media (WHO 162, 1994).
No degradation of PBBs by plants has been recorded. In contrast to plants, animals readily absorb PBBs (WHO 152, 1994). Data on environmental fate (although limited to MBDE, DiBDE, DeBDE) suggest that biodegradation is not an important degradation pathway for PBDEs, but that photodegradation may play a significant role (WHO 162, 1994).
Environmental studies so far indicate a high persistence of the original PBBs, or a partial degradation to less brominated congeners. Considering the diversity of micro-environments both laboratory and field data on photo alteration of PBBs are incomplete; there is a lack of studies on the photochemistry of PBBs in water, or in vapour or solid states. Because the carbon-bromine bond is less stable than the carbon-chlorine bond reductive debromination may be a degradative pathway of bromobiphenyls and this reaction may have toxicological consequences, not encountered with PCBs (WHO 152, 1994).

ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

PBBs

The only report (Stratton and Whitlock, 1979) about PBB levels in the air were air samples taken in the vicinity of 3 PBB plants in the USA. Traces of HxBB (0.06-1.10 ng/m^3) were found in 2 samples. Depending on its source, the predominant PBB compounds detected in surface water were HxBB and DeBB (WHO 152, 1994). Generally PBBs reach higher concentrations in sediments than in associated waters. River sediment close to a PBB plant is more contaminated with PBBs than up- or downstream sediments (WHO 152, 1994). A time-trend study of PBB levels of Pine River sediment shows that after termination of Fire Master BP-6 production PBB distributions and concentrations in the sediments not significantly change, showing persistence of PBB in the sediments (Hesse and Powers, 1978). Many studies started after the accidental contamination in 1973 in Michigan, with Fire Master FF-1 being inadvertently substituted for magnesium oxide in the production of cattle feed. Estimates on the amount of PBBs used vary between approximately 290 kg (Fries, 1985) to 1000 kg (IARC, 1978). PBBs were mixed into feeds, distributed widely to Michigan farmers. In addition, feeds not formulated to contain magnesiumoxide became contaminated (relatively low concentrations) due to carry over of PBBs from batch to batch through mixing equipment and, on farms, through the recycling of contaminated products. The mixing error was not discovered immediately, and it was almost a year before analysis indicated that a compound of PBB was involved in the illness or death of farm animals. During this time, contaminated animals and their products entered the human food supply and the environment of the state Michigan (WHO 152, 1994).
Groundwater near local disposal sites was not contaminated by PBBs (Shah, 1978). Soils from PBB industrial sites (2000 mg/kg dry weight, Fire Master plant) have in general been more heavily contaminated than Michigan soils (371 µg/kg dry weight) (Jacobs et al., 1978; Fries,

1985). Contamination of animal feed or foods by PBBs has been reported only in connection with the Michigan PBB incident (WHO 152, 1994).
Recent reports refer to PBB contamination in fish eating mammals and birds in Europe (table 7), and in the USA. Furthermore PBB residues were found in terrestrial mammals (reindeer 0.037 µg/kg lipid, 2,2',4,4',5,5-HxBB (BB 153) Jansson et al., 1993), freshwater and marine fish in Europe (Who 152, 1994). The pattern of PBB congeners found in fish differs in a characteristic manner, depending on the different capture sites. High levels of NoBB and OcBB (besides PBDE) were present in fish from German rivers (WHO 152, 1994). However HxBB were predominant in fish from the North Sea and Baltic Sea (Pijnenburg et al., 1995; WHO 152, 1994). In all samples from the Baltic Sea 3,3',4,4',5,5' HxBB was found in relative high concentrations (maximum concentration: 36 µg/kg fat), but it was not detected in the North Sea or rivers (Krüger et al., 1988). The concentration of other HxBBs were usually higher in fish from the Baltic Sea than in fish from the North Sea. Concentrations of BB 153 determined in marine fish ranged from 0.2 - 2.4 µg/kg lipid (Baltic fish) and in seals 0.4 (Northern Ice Sea)- 26 (Baltic Sea) µg/kg lipid (Krüger et al., 1988; Jansson et al., 1993). The congener pattern found in fish is quite different from that found in commercial products. Many of the major peaks could well be the result of photochemical debromination of DeBB, but this has not been confirmed (WHO 152, 1994).

Table 7. Total PBB and PBDE concentrations calculated as technical mixture equivalents in herring, seals and sea birds (µg/kg lipid)(from Jansson et al., 1987 and 1993).

		Σ-PBB		Σ-PBDE	
Organism	Area	1987	1993	1987	1993
Herring	Baltic Sea		0.16	49	528
	Bothnian Gulf		0.09	30	123
	Skagerrak		0.27	(17)	735
Seal	Baltic Sea	20/26		90	728
	Kattegat	3		10	
	Spitsbergen	4		40	
	Northern Ice Sea		0.42		51
Guillemot	Baltic Sea	160		370	
	North Sea			80	
	Northern Ice Sea	50		130	
Sea eagle	Baltic Sea	280		350	

Long range transport has not been proven, but the presence of these compounds in Arctic seal samples indicates a wide geographical distribution (WHO 152, 1994).
For most human populations, direct data on exposure to PBBs from various sources have not been documented. Occupational exposure was found in employees in chemical plants in the USA (skin contact and inhalation) and in farm workers (skin contact, inhalation, and contaminated food). Median serum and adipose tissue PBB levels were higher among chemical workers (WHO 152, 1994).
Recently, PBBs (and also PBDEs) have been detected in cow's milk and human milk in Germany (Krüger et al., 1988). The congener patterns in these samples differ from that found in fish. BB 153 was the most abundant component in human milk (Krüger et al.,1988). The

relative concentration of BB 153 is higher in human milk (1.03 µg/kg lipid, Krüger et al., 1988) than in fish (ranged between 0.092 - 24 µg/kg lipid, Krüger et al., 1988; Jansson et al., 1993). Total levels found in human samples were substantially higher than levels that were detected in cow's milk (both samples, cow and human from the same region, Krüger et al., 1988)). Thus, an infant of 6 kg body weight consuming human milk will have a higher intake of PBBs than an adult consuming cow milk, respectively 0.01 µg PBB/kg body weight per day and 0.00002 µg PBB/kg body weight per day (WHO 152, 1994).

PBDEs

In Japan a large amount of PBDEs was determined in the airborne dust, DeBDE observed being dominant (83 -3060 pg/m^3), other congeners were TeBDE, PeBDE, and HxBDE (Watanabe et al., 1995). These PBDEs were also present in two ash and soil samples from a recycling plant in Taiwan, in which DeBDE was the dominant congener (510 - 2500 µg/kg ash and 260 - 330 µg/kg soil, Watanabe, undated). In water samples from marine estuarine and river water (USA) only MBDE was detected (WHO 162, 1994).
In Germany tri- to heptaBDE were found at relatively high concentrations (0.39 - 15 ng/g, dry weight?) in sewage sludge (Hagenmaier et al., 1991). Two samples of sewage sludge from the same sewage treatment plant in Gothenburg (Sweden) were analysed. One sample was a pool of subsamples taken during a period with little rain (1) and the other was composed of subsamples during a rainy period (2). The levels were 25 and 21 ng/g dry weight for the dry and wet period respectively, indicating that the primary PBDE sources to this matrix are household and industrial effluent and not washout from the atmosphere (Sellström, 1996).
Surfacial sediment samples up- and downstream from a plastic industry in Sweden indicated this industry as the most likely source. The relative amounts in the analysed sewage sludge and surfacial sediments samples are quite similar to the pattern for the technical PBDE product Bromkal 70-5 DE (table 8)(Sellström, 1996). De Boer & Dao (1993) found a PBDE pattern in sediments, which is comparable to the pattern of this technical mixture. In these sediment samples PeBDE-concentrations were higher than the TeBDE-concentrations. TeBDE, PeBDE and HxBDE were found in sediments of Osaka Bay (Japan), and in 7 of 15 riverine and estuarine samples, DeBDE was found in higher concentrations (Watanabe and Tatsukawa, 1990), indicating accumulation of higher brominated congeners in the sediment. Recently DeBDE has been detected for the first time in Sweden in some sediment samples from the river Viskan and sludge samples (Sellström, 1996). The upper layer in a laminated sediment core from the Baltic Sea contained higher levels of TeBDE and PeBDE than lower layers, indicating an increasing burden of these compounds (Nylund et al., 1992, 1994). Other time-trend studies of Baltic sediments showed an increasing trend in the concentrations of PBDEs between 1973 and 1990 (Sellström, 1996). PBDEs seem to have a higher absorption to the sediment than PCBs (de Boer & Dao, 1993).

Table 8. Percentages of PBDE congeners of Bromkal 70-5 DE (from Sellström et al., 1990; Jansson et al., 1993).

	2,2',4,4'-tetra-BDE	penta-BDE (not defined)	2,2',4,4',5-penta-BDE
Bromkal 70-5 DE	44	8	48
Sewage sludge	40	9	51
Seal	89-92	3-5	2-6
Herring	62-80	6-11	9-21

Swedish results from freshwater fish studies (pike, perch, trout, bream, eel; table 9) indicate that southern Sweden may be more contaminated with PBDEs than northern Sweden (Sellström, 1996). Compared with levels found in terrestrial animals (rabbit, moose, reindeer respectively 0; 1.7; 0.47 ng/g lipid weight, Jansson et al., 1993) showed that the concentrations of PBDEs are higher in aquatic organisms than in terrestrial organisms (WHO 162, 1994; Sellström, 1996). Sellström (1996) and Watanabe et al. (1987) detected PBDEs in fresh water fish (Sweden and Japan) with TeBDEs congeners dominant in the samples. Comparing these results with Bromkal 70-5 DE the relative amount of TeBDEs is much higher (Sellström, 1996). In addition, de Boer and Dao (1993) found relatively higher concentrations of TeBDEs in biological samples. The PBDE pattern in sediments is more comparable to the pattern of Bromkal 70-5DE than the PBDE pattern in biological samples. Relatively higher TeBDEs concentrations in fish may be caused by a more rapid uptake of lower brominated compounds. It was suggested that a membrane barrier would exist for higher brominated compounds due to the larger size of these molecules. Therefore, in sediments relatively more higher brominated compounds may be expected (de Boer and Dao, 1993).

Table 9. PBDE concentrations in the environment (DW = dry weight; WW = wet weight; lipid = lipid basis. From Pijnenburg et al. 1995).

Matrix	Location	Concentration (μg/kg)	Compound	References
Sediment	Osaka Bay (Japan)	11–30 DW	tetra-, penta-, hexa-BDE	Watanabe and Tatsukawa (1990)
–	Rivers (Japan)	33–375 DW	deca-BDE	Watanabe and Tatsukawa (1990)
Mussels	Osaka Bay (Japan)	15 WW	tetra-BDE	Watanabe et al. (1987)
Cod liver	Northern North Sea	26 lipid	tetra-BDE	de Boer (1989)
–	–	3 –	penta-BDE	de Boer (1989)
–	Central North Sea	54 –	tetra-BDE	de Boer (1989)
–	–	6 –	penta-BDE	de Boer (1989)
–	Southern North Sea	170 lipid	tetra-BDE	de Boer (1989)
–	–	22–26 lipid	penta-BDE	de Boer (1989)
Herring	Southern North Sea	100 lipid	tetra-BDE	de Boer (1990)
Eel	Rur River	1.4×10^3 lipid	tetra-BDE	de Boer (1990)
Pike	Southwest Sweden	27×10^3 lipid	PBDE[1]	Sellström et al. (1990)
Pike liver	Southwest Sweden	110×10^3 lipid	PBDE[1]	Sellström et al. (1990)
Eel	Southwest Sweden	17×10^3 lipid	PBDE[1]	Sellström et al. (1990)
Trout and bream	South Sweden	100–170 lipid	tetra-BDE	Sellström et al. (1993)
Cormorant liver	Rhine Delta	28×10^3 WW	PBDE	de Boer (1990)
Baltic Guillemot egg	Baltic Sea	2×10^3 lipid	PBDE[1]	Sellström et al. (1993)
Osprey	–	$0.16–1.9 \times 10^3$ lipid	PBDE[1]	Sellström et al. (1993)
Ringed Seal	Northern Ice Sea	51 lipid	PBDE[1]	Sellström et al. (1993)
Baltic Grey Seal blubber	–	728 lipid	PBDE[1]	Sellström et al. (1993)
Seal blubber	Baltic Sea	730 lipid	PBDE	Andersson and Blomkist (1981)
–	–	26 lipid	tetra-BDE	Andersson and Blomkist (1981)

[1]Mainly tetra-BDE.

The main PBDE-load in Dutch freshwater ecosystems originates from Germany, which is indicated by the higher concentration of TeBDEs in eel from the river Rhine compared to other Dutch freshwater systems. Most temporal trend graphs show decreasing trends, although a stabilisation is visible in eel from the river Rhine and Meuse since 1988/1989. Concentrations of PBDEs in the river Rur have increased, possibly caused by the use of PBDEs in hydraulic mining equipment in Germany (de Boer and Dao, 1993). This usage seized in 1990, but only a slight decrease in PBDEs levels has been observed since.
Noticeable concentrations of PBDEs were determined in carp of three age classes collected from the Buffalo river (New York, USA). TeBDEs accounted for 94-96% of total PBDE concentrations (Loganathan et al., 1995).
A spatial trend for PBDEs, detected in herring from different places along the Swedish coast, is almost identical to that previously found for PCB and DDT. The concentration is the lowest on the Swedish west coast and the highest in the southern part of the Baltic Sea. The concentration then decrease from south to north (Sellström, 1996). TeBDEs concentrations in herring from the Skagerrak were comparable to TeBDEs concentrations in North sea fish (Central and North). TeBDEs concentrations (cod liver) decreased from the southern part to the northern part of the North Sea (Pijnenburg et al., 1995). Temporal studies on TeBDE in cod liver from the North Sea show a slightly decreasing trend (figure 5). However, the number of samples is very limited (de Boer and Dao, 1993). As in Europe, in Japan TeBDEs are the major component in marine and shellfish samples (Watanabe et al., 1995).

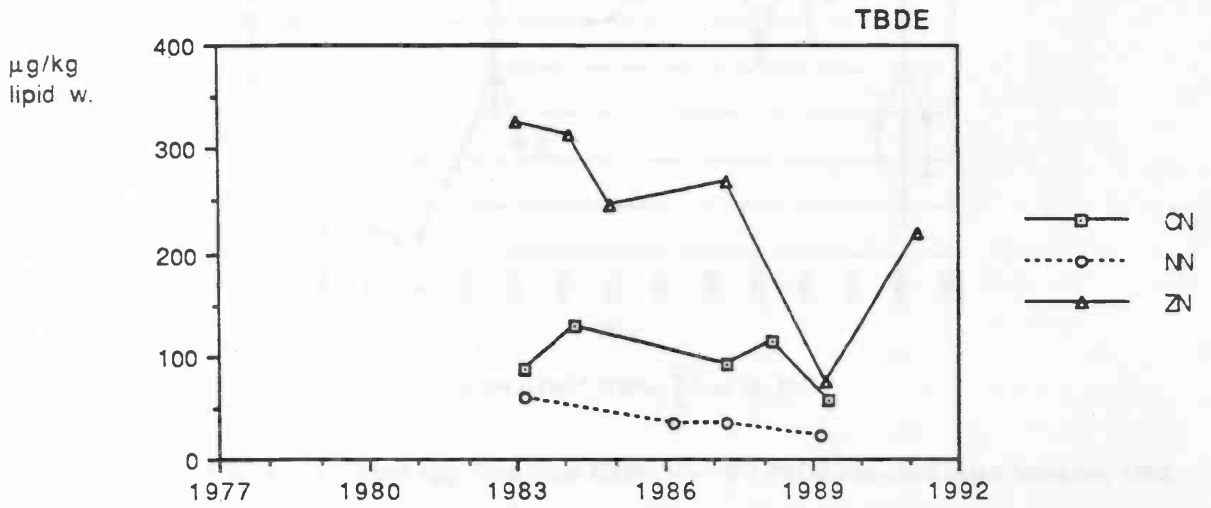

Figure 5. Temporal trend of TeBDE in cod liver from the northern (NN), central (CN) and southern North Sea (ZN) (from de Boer and Dao, 1993).

Contamination of PBDEs on lipid weight basis is about nine times higher in herring caught in spring than herring caught in autumn. This relationship has previously been shown for PCB, DDT and dioxins. Spring herring is caught near the breeding season and this probably affects lipid disposition and metabolism, which in turn may affect concentrations of organohalogens (Sellström, 1996).
Several fish eating animals were studied. Extremely high PBDEs levels (upto 25,000 µg/kg TeBDE and 4,000 µg/kg PeBDE (wet weight)) were found in organs of a cormorant from the Rhine delta. Since this is based on only a single animal, further research is necessary (de Boer and Dao, 1993). The PBDEs levels found in an osprey from Sweden, which also feeds on

freshwater fish, were high as well (0.16 - 1.9 x 10^3 µg/kg lipid, Sellström, 1996). Baltic seals contained higher TeBDEs concentrations than the North Sea seals (de Boer and Dao, 1993). Time-trend studies of guillemot eggs (Stora Karslö, Baltic Sea, Sweden) indicate that the levels of PBDEs have increased since 1970 (figure 6) and that this increase is significant. A similar time-trend study of pike (from Lake Bolmen, Sweden) shows a similar trend. However, in guillemot eggs there are indications that the PBDEs levels may have decreased during the last years (Sellström, 1996). Table 7 shows more studies, both the total PBDE concentrations and total PBB concentrations are given. Both guillemot and grey seals show higher concentrations of the three PBDE congeners, 2,2',4,4' TeBDE, an unknown PeBDE, and 2,2',4,4',5 PeBDE than the herring they feed on. TeBDE seems to biomagnify to the relatively highest extent. This indicates that PBDEs biomagnify (Sellström, 1996). Biomagnification is also observed in dolphins and porpoise from the southern North Sea and the Atlantic west of Ireland. Biomagnification factors between fish and investigated marine mammals are approximately 10-30 (de Boer and Dao, 1993).

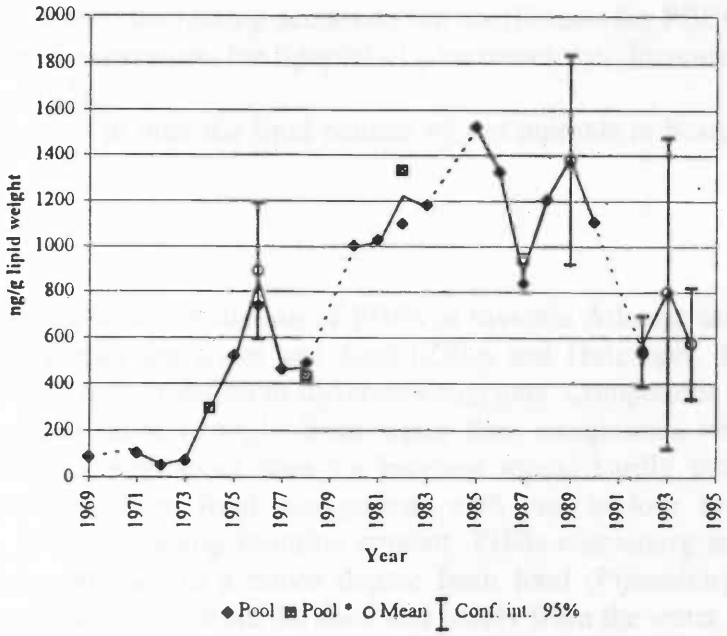

Figure 6. Time-trend study of guillemot eggs from Stora Karlsö, sum of 3 PBDE congeners (from Sellström, 1996).

Only long range transport through air can explain the contamination in whitefish in Lake Storvindel, Sweden. PBDEs have been found in an air sample collected near this lake. In another air sample collected at the southern part of the Baltic Sea PBDEs were detected as well (Sellström, 1996).

In Germany cow's milk was analysed and an average concentration of 3.57 µg/kg fat (4 samples) was found and determined as Bromkal 70-5 DE, main component HxBDE. PBDEs were also detected in breast milk (Germany). The samples contained 0.6-11.1 µg PBDE/kg fat, determined as Bromkal 70-5DE, and the main component was HxBDE (Krüger et al., 1988). Uptake of TeBDEs and PeBDEs may occur in humans via the foodchain, e.g. by consuming fish. Exposure may also occur through skin contact (flame retardants in polymers used in textiles) and via inhalation (WHO 162, 1994).

TOXICOKINETICS

PBBs and PBDEs are distributed throughout the animal species and human beings, the highest equilibrium concentration being in adipose tissues. Relatively high levels have been found in the liver, particularly of the more toxic congeners, which appear to be concentrated in the liver (WHO 152, 1994; WHO 162, 1994). In the environment BDE congeners tend to accumulate in the tissue of marine mammals and birds as long as their molecular structure is not to large to prevent them from entering the cells (Greve et al., 1996). Animals and humans eliminate PBBs and PBDEs mainly through faeces. Another pathway of elimination is through milk. In mammals, transfer of PBBs to offsprings occurs through transplacental and transfer lactation (WHO 152, 1994; WHO 162, 1994).
Using K_{ow} (log K_{ow}, table 2A and 2B), the accumulation potential of organic compounds can often been estimated successfully. Compounds with a high K_{ow} usually have a high affinity for animal lipids (Pijnenburg et al., 1995). As expected from their high lipophilicity, PBBs and PBDEs show a marked tendency to accumulate in animals and humans. Zitko and Hutzinger (1976) described decreasing accumulation coefficients for PBBs with an increasing bromine substitution. Furthermore, the lipophilicity increases with increasing bromine content (Pijnenburg et al., 1995).
It is obviously important to note the lipid content of test animals in bioaccumulation studies (WHO 152, 1994).

PBBs

In laboratory studies on bioaccumulation of PBBs in juvenile Atlantic salmon (*Salmo salar*) PBB was supplied through the water and food (Zitko and Hutzinger, 1976; Zitko, 1977). There are differences in accumulation of different congeners. Compounds with a low bromine content bioconcentrated more strongly from water than compounds with a high bromine content. PBB congeners with more than six bromine atoms hardly bioconcentrated at all (Zitko, 1977). However, from food, compounds with one to four bromine atoms were accumulated more with increasing bromine content. PBBs containing six to eight bromine atoms were only accumulated to a minor degree from food (Pijnenburg et al., 1995). 3,4 DiBB was not accumulated at all from the food and hardly from the water. The corresponding 3,4 DiCB shows the same effect (Zitko, 1977). No explanation was given for this phenomenon. There is shown for PCBs that solubility of the different congeners depends on chlorine substitution at the *ortho* position. Because 3,4 DiCB has no *ortho*-Cl, low solubility in water of these congeners may be the reason for low accumulation (Bruggeman et al., 1992). Furthermore HxBBs were found in fish tissue after exposure to a diet spiked with only OcBBs (Zitko, 1977). Such a dehalogenation is unknown for higher chlorinated . The accumulation of Fire Master from food appeared to be higher than the accumulation of other PBBs (Pijnenburg et al., 1995).
A half life of approximately 69 weeks was calculated for the elimination of 2,2',4,4',5,5' HxBB from the body fat of rats. A half life of more than 4 years was found in rhesus monkeys (WHO 152, 1994). The half life of two PBB congeners, Fire Master and the technical OcBB was determined in fish (table 10, Zitko, 1977). A study to determine the half life of PBBs in human sera concluded that the estimated half life of a given PBB mixture in humans is approximately 11 years, although a lot of variation was observed. Thus, the body burden of PBB exposed people, in the absence of other exposures, will decrease only gradually over time. Persons with an initial level of 45,5 ppb of PBBs will take more than 60

years before their PBB levels to fall below the current detection level of 1 ppb (Rosen et al., 1995).

Table 10. Biological half lives of PBBs in fish, following uptake from food or water (from Zitko, 1977).

Compound	Uptake from water	Uptake from food
2,2',4,5' tetra-BB	21 d	28 d
2,4',5 tri-BB	13 d	26 d
Firemaster	n.a.	93 d
OB	n.a.	93 d

PBDEs

As stated before, a marked bioaccumulation of TeBDE was found in fish and fish eating animals in the environment. The relatively higher TeBDE concentration in fish may be caused by a more rapid uptake of lower brominated compounds (de Boer and Dao, 1993). This may be explained by decreasing membrane passage velocity of bromodiphenyl ether molecules with increasing bromine content (De Boer and Dao, 1993; Von Meyerinck et al., 1990).
The hypothesis is that the highest brominated compounds like DeBDE can hardly pass the cell membrane and therefore are not able to bioaccumulate.
In a laboratory study which investigated the metabolism of 2,2',4,4'-TeBDE, mice and rats were dosed orally with ^{14}C-labelled 2,2',4,4'-TeBDE. There is evidence that in rats 2,2',4,4'-TeBDE metabolised at a very low rate. 86 % of the dose remained in rat tissues 5 days after exposure. In contrast, excretion of 2,2',4,4'-TeBDE in mice was much more rapid with 53 % of the dose excreted after 5 days. The major excretory pathway is via urine. This indicates that water soluble metabolites were formed, but their structure is not yet elucidated. This implies that 2,2',4,4'-TeBDE can be metabolised by some organisms. In this study the high concentration of irreversibly bound metabolites in the mouse lung is notable (Klasson-Wehler et al., 1996).
In a laboratory study on the accumulation of PBDE, carp was exposed for 8 weeks to different PBDE compounds. Exposure to commercial PeBDE at 10 or 100 µg/litre showed a bioconcentration factor of more than 10.000. Higher brominated compounds lead to little bioaccumulation in carp with a bioconcentrationfactor < 4 (CBC, 1982).
DeBDE is absorbed poorly from the gastrointestinal tract (approximately 1% in rats) (WHO 162, 1994). It was found that the gastrointestinal absorbtion of PBBs varies according to the degree of bromination (the lower brominated compounds being more easily absorbed) (WHO 152, 1994). Studies on the gastrointestinal absorbtion of DeBDE concluded no accumulation of DeBDE. Recently a study about the uptake of DeBDE in rainbow trout via administration in the diet, resulted in different conclusions. It was shown that DeBDE is bioavailable from the gastrointestinal tract. Furthermore DeBDE tissue levels decreased during depuration, but persistent tissue levels of 2,2',4,4',5,5' HxBDE after depuration was attributed by the authors to metabolisation of DeBDE. This indicates that DeBDEs can contribute to the bioaccumulation of PBDEs, but not as fast as lower brominated isomers (Kierkegaard et al., 1995).
The half life of Bromkal 70-5 DE in perirenal fat was investigated in groups of 3 male and 3 female Wistar rats. The results are shown in table 11 (Meyerinck et al., 1990).

Table 11. Half lives of PBDE in male and female rats (from Meyerinck et al., 1990).

PBDE	halflives in female rats (in days)	halflives in male rats (in days)
HxBDE[1]	44,6	55,1
HxBDE[2]	90,0	119,1
PeBDE[1]	47,4	36,8
PeBDE[2]	25,4	24,9
TeBDE	29,9	19,1

1 &2 means different isomers, confidence interval, P=0,05

PCBs and PCBEs have accumulation factors of approximately the same magnitude. The validity of this relation has not been confirmed for PBBs and PBDEs. PBBs and PCBs with 1 to 4 bromine or chlorine atoms have accumulation factors of approximately the same magnitude, but PBBs with more than 5 bromine atoms accumulate less than the corresponding PCBs (Pijnenburg et al., 1995).

Biotransformation

Reactions involved in the process of biotransformation have been subdivided in so-called phase I (modification or transformation reactions) and phase II (conjugation reactions). Superlipophilic compounds accumulate mainly in the fatty tissues, but lipophilic compounds can be biotransformated. Modification changes lipophilic compounds in polar or reactive compounds. These polar compounds will be hydrophile or reactive compounds after conjugation (phase II). A hydrophile compound will be eliminated via faeces and urine, but the reactive compound binds covalently to tissue components. These biochemical transposition of xenobiotics results in changes, not only in chemical and physical properties, but also in toxicological properties. The most important enzymsystem for oxidation of xenobiotics in phase I, is the Cytochrome P450 family. This system is mainly found in the liver, and consist of enzymes that supply electrons, which are needed in oxidation. It further consist of the Cytochrome P 450 enzyme component, which is a haem protein. PBBs are porphyrinogenic compounds, meaning they interfere with the production of haem and proteins (Temmink and Rietjens, 1996).
Qualitative, the structure effect relationships for BB congeners show a high similarity with those of CB (Pijnenburg et al., 1995). Quantitatively, bromine substitution appears to have a more pronounced effect than chlorine substitution in inducing the P450 IA subfamily (3-MC

type inducer) (Andres et al., 1983). This may be due to a higher affinity of BB congeners for the cytosollic Ah receptor (Pijnenburg et al., 1995). Also the mechanisms of toxicity of PBDEs are similar to those of the chlorinated dibenzodioxins and PCBs (Pijnenburg et al., 1995; Hanberg et al., 1991). They exert most of their toxic effects through the same Ah receptor (Hanberg et al., 1991).

The main component of Firemaster BP-6 and FF-1,2,2',4,4',5,5'-HxBB (BB 153), is a PB (phenobarbital) type inducer, i.e. it induces the P450 IIB subfamily. 2,2',3,4,4',5,5'-HpBB (BB 180) is the same type of inducer. 3,3',4,4'-TeBB, 3,3',4,4',5-PeBB and 3,3',4,4',5,5'-HxBB (respectively BB 77, BB 126 and BB 169) are pure 3-MC (3-methylcholanthrene) type inducers. These PBB congeners are the main components of the Fire Master products and it has been shown that these BB congeners are entirely responsible for inducing the mono oxygenase (MO) system in rats (Aust et al., 1987), other contaminants in these products do not play a significant role (Pijnenburg et al., 1995).

A PBDE mixture of low overall bromination and a mixture of high overall bromination, both induced two enzymes which catalyses the conjugation in phase II metabolism (*O*-ethyl-*O*-*p*nitrophenyl phenylphosphothionate and Uridine Diphosphate-glucuronyltransferase).The enzymes *p*-nitroanisole demethylase and arylhydrocarbon hydroxylase were induced relatively stronger by the lower brominated mixture (Carlson, 1980 a & 1980b). A long-term study in rats show that these inducers are not only potent but that their effect could be long-lasting. The DeBDE congener (BB 209) did not cause any enzyme induction (Carlson, 1980b).

No biotransformation of 2,2',4,4'-TeBDE, 2,2',4,4',5-PeBDE and DeBDE investigated in microsomal preparations of livers of marine mammals and birds, was observed in the *in vitro* bioassays. Thus the observed enrichment of lower brominated congeners in residues of marine biota is most likely due to higher uptake rates. Although PBDEs seem to have affinity to the same biological receptors as the PCBs, they did not inhibit metabolisms of CB congeners used as positive control (Greve et al., 1996).

Many PBB congeners are persistent in biological systems. There was no evidence of significant metabolism or excretion of more abundant components of the Fire Master mixtures nor for OcBB and DeBB. *In vitro*-metabolism studies showed structure-activity relationships for the metabolism of PBBs. PBBs could be metabolized by PB-induced microsomes only if they possessed adjacent non-brominated carbons, *meta* and *para* to the biphenyl bridge on at least one ring (Moore et al., 1980; Mills et al., 1985; Dannan et al., 1986). Metabolism through 3-MC-induced microsomes required adjacent non-brominated *ortho* and *meta* positions on at least one ring of lower substituted congeners and higher bromination appeared to prevent metabolism (Mills et al., 1985). Hydroxylated derivates as major *in vitro*- and *in vivo*-metabolism products of lower brominated have been identified in vertebrates. The metabolic yield was relatively low. The hydroxylation reaction probably proceeds via both arene oxide intermediates and by direct insertion (WHO 152, 1994).

TOXIC EFFECTS

PBBs

Toxic effects on organisms in the environment

Most available data about the effects of PBBs on organisms in the environment are data on farm animals from the Michigan disaster. The estimated average exposure of cows at a high contaminated farm was 250 mg/kg body weight (Fries, 1985). A few weeks after ingestion of contaminated cattlefeed, clinical signs were a reduction, around 50%, in feed consumption (anorexia) and a decrease, around 40%, in milk production. Some cows showed an increased frequency of urination and lacrimation, and developed haematomas, abscesses, abnormal hoof growth, lameness, alopecia, hyperkeratosis, and cachexia. Several cows died within 6 months of exposure (Jackson and Halbert, 1974). The death rate in 6- to 18- months old calves was much higher, 50% died within 6 weeks (Jackson and Halbert, 1974; Robertson and Chynoweth, 1975).
In contrast of the observed toxicity in cattle in Michigan, in the Michigan population no definitive health effects that could be correlated with PBB exposure have been identified. However, the follow up period has not been long enough for the development of cancer. In industry it appears that chloracnelike lesions may develop in workers producing PBB, and hypothyroidism in workers exposed to DeBB (WHO 152, 1994).

Laboratory experiments

Further *in vitro* studies were necessary to identify toxic effects of PBBs. Controlled long term feeding studies on cattle exposed to low doses of Fire Master did not reveal any adverse effects as indicated by food intake, clinical signs, clinicopathological changes, or performance. Minks, guinea-pigs, and monkeys appeared to be more suspectable to PBB toxicity (WHO 152, 1994).
Fire Master BP-6 appears to have a similar acute toxicity to rats as the PCB mixtures Aroclor 1254 and Kanechlor 500 (table 12, Pijnenburg et al. 1995). The LD_{50} values of commercial mixtures show a relatively low order of acute toxicity (LD_{50} > 1 g/kg body weight) in rats, rabbits and quails, following oral or dermal administration. The toxicity of PBBs was higher with multiple dose rather than single dose administration. The few studies performed with commercial OcBB and DeBB mixtures didn't result in mortality in rats and fish. On the basis of limited, available data, OcBB and DeBB appear to be less toxic and less absorbed than other PBB mixtures (WHO 152 1994).

Table 12. Acute toxicities of PBB and PCB. AHH = aryl hydrocarbon hydroxylase activity ([1] Gupta et al., 1983; [2] Andres et al., 1983; [3] Safe, 1984).

Mixture	Species/Sex	Details	$LD_{50}/EC_{50}/LC_{50}$
Firemaster BP-6 (PBB)	Rat (F)		LD_{50}: 65 mg/kg/d[1]
Firemaster BP-6 (PBB)	Rat (M)		LD_{50}: 149 mg/kg/d[1]
Firemaster BP-6 (PBB)	Rat	AHH activity	EC_{50}: 50–55 mg/kg[2]
Aroclor 1254 (PCB)	Rat	AHH activity	EC_{50}: 50–55 mg/kg[2]
Kanechlor 500 (PCB)	Rat	AHH activity	EC_{50}: 50–55 mg/kg[2]
Firemaster BP-6 (PBB)	Rat	Oral	LD_{50}: 21.5 g/kg[3]
Hexa-BB	Rabbit	Skin	LD_{50}: 5 g/kg[3]
Firemaster FF 1 (PBB)	Mink	Food	LC_{50}: 3.95 mg/kg[3]

The toxicity of PBB congeners strongly depends on their molecular structure (WHO 152, 1994; Pijnenburg et al., 1995). Induction of the P450IA subfamily of P450 is the precursor of a whole spectrum of possible effects at more integrated levels of biological structure: weight loss, thymus atrophy, and changes in the liver such as proliferation of the smooth endoplasmatic reticulum (location of the P450 system), increased RNA and protein content, decreased DNA content, cell necrosis, liver enlargement, and hepatic porphyria (Koster et al., 1980; Render et al., 1982; Jensen et al., 1983).
The more toxic congeners cause a decrease in thymus and/or body weight and produce pronounced histological changes in the liver and thymus. Categorization of halogenated has been made on a structural basis. Category 1 comprises isomers and congeners lacking *ortho*-substituents (coplanar PBBs). Mono-*ortho*-substituted derivates constitute the second category. Other PBBs (mainly those with two or more *orhto*-bromines) have been organized into the third category. Congeners of Category 1 tend to elicit the most severe effects, while the congeners of the second and third categories show decreasing toxicological changes. Within these categories, the degree of bromination may also influence toxicity.
In all combinations tested, 3,3',4,4',5,5'-HxBB was found to be the most toxic PBB (WHO 152, 1994).
A review on the carcinogenicity of PBBs and PCBs (Silberhorn et al., 1990) concluded that there are strong indications that these compounds, (and other related compounds), are not mutagenic compounds but do promote the carcinogenicity of mutagenic compounds, such as nitrosamine and certain polyaromatic hydrocarbons (PAHs)(Jensen et al., 1983; Safe, 1984; Kavanagh et al,. 1985). In marine environment halogenated compounds often co-occur with PAHs. Tumor promoting ability has been reported for 3-MC type inducers as well as PB-type inducers (Pijnenburg et al., 1995)
The only lifetime study with technical NoBB mixture was conducted on rats and mice in a recent bioassay. The lowest dose tested that still produced carcinogenic effects on rodents was 0.5 mg/kg body weight per day (orally), and no observed effect level in a rat was 0.15 mg/kg body weight per day (Momma, 1986). The carcinogenicity of technical OcBB and DeBB has not been studied, although a number of chronic effects have been observed in experimental animals at doses of around 1 mg/kg body weight per day during long term exposure (WHO 152, 1994).
After the ingestion of a Fire Master mixture, hyperkeratosis and hair loss were seen in cattle, and lesions resembling chloracne were seen in rhesus monkeys (50 mg/kg in the diet) (Safe, 1984). After 20 wk, exposure at a dose of 2 mg/animal twice weekly, Fire Master FF-1 also caused skin papillomas in previously initiated mice (Poland et al., 1982).
Fire Master BP-6 caused chronic and subchronic neuronal symptoms, such as irritation, changed behaviour and decreased muscular control (Safe, 1984). Immunosuppression by PBBs occurs at levels that also cause a number of the other toxic effects described (Pijnenburg et al., 1995).
In the article of Pijnenburg it is noted that in monkeys Fire Master FF-1 caused a longer sexual cycle, and that PBB caused decreased egg production and nesting behaviour in Japanese quail (Aust et al., 1987). One recent study reported that in mice PBB (2-BB and 4-BB) reduced the *in vitro* fertilization rate at higher dosages. Furthermore, an increased incidence of abnormal two-cell embryos and degenerative öocytes was observed at the 1 and 10 µg/ml concentration of PBB (Kholkute et al., 1994).
PBBs also affect the regulation of steroid hormones. The extent depends on the species as well as the dose and duration of exposure. Furthermore, PBBs interact with thyroid hormone production e.g. rats and pigs showed dose related decreases in serum thyroxine and

triiodothyronine (WHO 152, 1994). PBBs produced porphyria in rats and male mice at doses as low as 0,3 mg/kg body weight per day (no observed effect level was 0,1 mg/kg body weight per day). There was a pronounced influence of PBBs on vitamin A storage as well as effects on intermediary metabolism (WHO 152, 1994).

PBDEs

There is no information available on the toxicity of PBDEs in organisms in the environment. Commercial DeBDE, OcBDE and PeBDE have been the subject of laboratory toxicological studies. Toxicological data on one of these compounds do not reflect the toxicity of all PBDE congeners. The acute toxicity of DeBDE and OcBDE for laboratory animals is low (LD_{50} > 1 g/kg body weight). The acute oral toxicity of PeBDE is low in rats, and dermal toxicity in rabbits is also low. DeBDE and OcBDE are not irritant to the skin, and DeBDE is not irritant to the eyes of a rabbit, but OcBDE gives minor eye irritation (WHO 162, 1994).
DeBDE has no effect on survival, body weight or food consumption, and no gross or microscopic pathological effects in feeding studies on rats and mice have been found (WHO 162, 1994). However in short therm toxicity studies with OcBDE, rats administered dietary levels of 100 mg/kg had increased liver weights and showed microscopal changes of liver tissue. These liver changes were more severe at higher dose levels, i.e., 1000 and 10,000 mg/kg diet. In addition, hyperplasia of the thyroid was seen (Great Lakes Chemical Corporation, 1987). Similar observations have been reported for PeBDE (WHO 162, 1994) and DeBDE (Norris et al., 1975). PeBDE increased liver/body weight ratio with 64%, OcBDE with 45%, and DeBDE with 25% in a study where a dose of 0.1 mM/kg per day was administered to male rats during 14 days (Carlson, 1980a). Further more PeBDE increased cytochrome P450 to a higher extend than OcBDE, while DeBDE didn't significantly increase cytochrome P450. As with BB congeners, the toxicity of BDE congeners strongly depends on their molecular structure, and BDEs induce the same isoenzymes of cytochrome P450 (Pijnenburg et al., 1995).
In a carcinogenicity study in rats and mice, DeBDE was administered at dietary levels of up to 50 g/kg. An increased incidence of adenomas (but no carcinomas) was found in the livers of male rats receiving 25 g/kg and female rats receiving 50 g/kg. In male mice, increased incidences of hepatocellular adenomas and/or carcinomas (combined) were found at 25g/kg and an increasing thyroid follicular cell adenomas/carcinomas (combined) at both dose levels. Female mice did not show any increase in tumour incidence. There was equivocal evidence for carcinogenicity in male and female rats and male mice only at dose levels of 25-50 g DeBDE/kg diet (NTP, 1986; Huff et al., 1984). Since the results of all mutagenicity tests have been negative, it was concluded that DeBDE is not a genotoxic carcinogen (WHO 162, 1994). In 1990 the International Agency for Research on Cancer (IARC) concluded that there was limited evidence for carcinogenicity, indicating that DeBDE, at present exposure levels, does not present a carcinogenic risk for humans (WHO 162, 1994).
The results for mutagenicity of PeBDE and DeBDE were negative. Results of the mutagenicity tests of OcBDE including an unscheduled DNA assay, *in vitro* microbial assays, and an assay for sister chromatid exchange with Chinese hamster ovary cells were also negative (Great Lakes Chemical Corporation, 1987).
DeBDE caused no teratogenic response in fetuses of rats intubated with 10-1000 mg/kg per day on gestation days 6-15. Fetal toxicity only occurred at 1000 mg/kg as subcutaneous edema and a delayed ossification of normally developed bones of the fetal skull (Norris et al., 1975). At high dose levels of OcBDE (25 and 50 mg/kg body weight) in rats, resorptions or delayed

ossification of different bones and fetal malformations were observed (Great Lakes Chemical Corporation, 1987). In rabbits there was no evidence for teratogenic activity, but fetotoxicity was seen at a maternally toxic dose level of 15 mg OcBDE/kg body weight (no observed effect level 2.5 mg/kg body weight) (Breslin et al., 1989). Test results for teratogenicity of PeBDE were negative (WHO 162, 1994). Oral administration of a dietary dose of approximately 0.5 mg Bromkal 70-5 DE for 3,5 months to female sticklebacks, *Gasterosteus aculeatus*, resulted in a decreased spawning success (Holm et al., 1993).

CONCLUSIONS AND DISCUSSION

In the industry brominated flame retardants are appreciated because of their high resistance towards acids, bases, heat, light, and reducing and oxidizing agents. When these products eventually reach the environment this high resistance becomes a clear disadvantage. Both PBBs and PBDEs are stable, lipophilic and persistent. The various congeners of these compounds differ in chemical and physical properties, which cause complex problems in the analysis. The synthesis of pure congeners for use as standard is a prerequisite for progress in chemical analysis as well as research into toxicological and biological effects. Only quantification of individual congeners will allow comparative studies.
The advantages for the industry in using PBBs and PBDEs as additive flame retardants still results in increasing production of these products. There are several alternatives, like non-halogenated products or reactive flame retardants, but the risks of these products are insufficiently studied. There is no information available proving these products as less harmful alternatives than brominated flame retardants.
Some PBB and PBDE products are precursors of toxic PBDFs and/or PBDDs in combustion processes. Under certain pyrolysis conditions it is possible to incinerate products with PBBs and PBDEs without the formation of toxic compounds. Nevertheless, little is known about the toxicity of PBDFs and PBDDs. It is estimated to be in the same order as that of PCDDs and PCDFs. Furthermore, in a fire situation the toxicity of brominated offgasses will be overshadowed through the toxicity and volume of carbon monoxide.
Further disadvantages in the use of PBBs and PBDEs as flame retardants are that during production and with their use as a synergist additive in plastics the heavy metal antimonyoxide is necessary, and recycling of products with PBBs and PBDEs is complex, if not impossible.
A considerable part of the PBBs and PBDEs produced will ultimately reach the environment due to the high stability of these compounds. Once introduced into the soil, PBBs and PBDEs do not appear to be translocated readily. PBB and PBDE congeners with lower bromine content are more easily distributed in the aquatic environment. It is suggested that photodegradation and debromination by micro-organisms may play a significant role in transformation of PBBs and PBDEs in the environment.
Both PBBs and PBDEs bioaccumulate. PBBs and PBDEs are found in environmental and human samples, even at large distances from known point sources. The PBB congener pattern in the environmental samples (e.g. fish and fish-eating animals) does not match those found in the technical products, which indicates environmental alterations, possibly by selective uptake or by photochemical debromination. The PBDE congener pattern in fish differs from the pattern in commercial PBDE mixtures. In fish higher concentrations of TeBDE were found. It was suggested that a membrane barrier exists for higher brominated compounds, due to the larger size of these molecules. Therefore in sediments a relatively higher level of higher

brominated compounds can be expected. HxBDE and lower brominated PBDEs have the potential to bioaccumulate in the environment. Studies by Klasson-Wehler and Kierkegaard showed that 2,2'4,4'-TeBDE can be metabolised by some organisms and DeBDE can be accumulated, but not as fast as lower brominated isomers.
DeBDE appears to be a less toxic material than PBBs. However, DeBDE is suspected to have a tendency to degrade to lower PBDEs. It is possible that these degraded compounds may pose environmental problems similarly to those of the lower brominated PBBs. In addition, pyrolysis of PBDEs produce larger amounts of dioxins and furans than PBBs. These findings culminate in the notion that DeBDE may not be as harmless as it was regarded in the past.
Different congeners behave differently in the environment and show large differences in toxicity. PBBs are extremely persistent in living organisms and have been shown to produce chronic toxicity and cancer in animals, although the acute toxicity is low. The acute toxicity of PBDEs is very low, and there is minimal information on the toxicity of PBDEs to living organisms.
Due to an insufficient amount of data, it may be only tentatively concluded that the present concentrations of PBBs and PBDEs, particularly in marine and fresh water food chains appear to represent a significant environmental risk. PBBs and PBDEs can be considered to be a potential threat for human health, particularly through fish consumption.
The main environmental properties and mechanisms of toxicity of the PBBs and PBDEs are likely similar to those of the structurally related PCBs and other aromatic organohalogen chemicals. Nevertheless the information about PBBs and PBDEs is scarce and although there is some degree of comparability to e.g. PCBs they are not the same. Assumptions have to be made with great care, certainly about their risk for the environment. PBBs are more similar to PCBs than PBDEs are, because of the oxygen atom between both ring in the latter.
Studies so far have shown that most of the PBB and PBDE congeners found in commercial flame retardants are persistent, lipophilic and bioaccumulating. Therefore, PBBs and PBDEs should no longer be used commercially and have to be replaced by environmentally less harmful alternatives. In the mean time, environmental exposure should be minimized through the appropriate treatment of effluent and emissions in industries using the compounds or products. The control of dust during manufacture and use should adequately reduce the risk for workers. Disposal of industrial wastes and consumer products should be controlled, to minimize environmental contamination with this persistent material and its breakdown products (like PBDDs and PBDFs).

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