POLYBROMINATED BIPHENYLS (PBB)

Chemical form

PBBs are a class of brominated hydrocarbons with a basic structure consisting of two phenyl rings to which bromine atoms are attached. There are 209 possible compounds, referred to as PBB congeners, which differ in the number and position of the bromine atoms in the two phenyl rings. Like polychlorinated biphenyls (PCBs), the benzene ring can rotate around the central bond that connects both phenyl rings adopting a planar and a non-planar configuration depending on the degree of substitution in the *ortho* positions. PBBs where the hydrogen atoms in the *ortho* positions are substituted by bromine atoms are called *ortho* PBBs, and those where the hydrogen atoms in the *ortho* positions are not substituted by bromine are called non-*ortho* PBBs. This difference in molecular structure is relevant for the interaction with different receptors determining the toxicological properties of PBBs (EFSA, 2010).

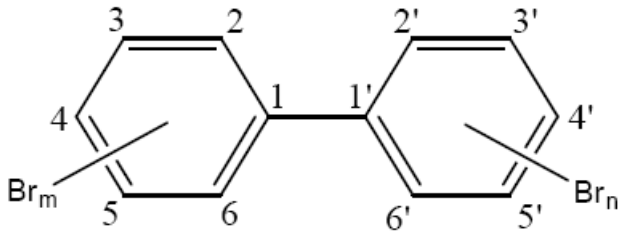

Figure 1: General structure of the PBB congeners (EFSA, 2010)

Contamination source

PBBs are additive flame retardants which were applied in synthetic fibers and polymers. As they are not chemically bound to the polymers, they can leach into the environment.

PBBs were produced until the mid 1980s, except decabromobiphenyl (DecaBB) which was produced in France up till 2000 (EFSA, 2010).

PBBs are lipophilic compounds with a low vapour pressure and low water solubility which decreases with increasing degree of bromination. They are generally chemically stable, persistent in the environment and bioaccumulative. It has been reported that higher brominated biphenyls can undergo photolysis and reductive debromination, thereby producing lower brominated congeners (EFSA, 2010).

Analytical method

The analysis of PBBs shows strong similarities to that of PCBs and PBDEs. In fact, the PBB analysis is often adapted from methods for PCBs or PBDEs. The congeners reported in several studies include BB-26, -29, -31, -49, -52, -80, -101, -103, -133, -135, -140, -153, -154 and -155 (Luross et al., 2002; von der Recke and Vetter, 2008).
Gas chromatography (GC) is the method of choice for instrumental separation of PBBs. The major difference between the methods for the determination of PCBs and PBBs arises from the lower volatility of PBBs compared to PCBs. Due to the lower volatility of PBBs, the GC method is performed at a higher temperature and low liquid-phase load of the stationary phase (EFSA, 2010).

Toxicity

Main targets of PBB toxicity were the liver, thyroid hormone homeostasis and the reproductive, nervous and immune systems.

Acute toxicity

PBBs have low acute oral toxicity, with lethal dose (LD50) values > 1,000 mg/kg body weight (bw) after single exposure. After repeated exposure (60 days), lethality was in the range of 65-150 mg/kg bw.

Carcinogenicity
PBBs are carcinogenic in the liver of rodents, by a non-genotoxic mode of action, which is assumed to have a threshold in the dose-response curve. A no-observed-effect level (NOEL) for hepatocarcinogenesis of 0.15 mg/kg bw has been identified in a long-term NTP study (1993) with Firemaster FF-1. There is evidence that *ortho* substituted congeners may cause cancer through interaction with nuclear receptors, such as the constitutive androstane receptor (CAR), whereas the non-*ortho* congeners appear to cause tumours as a consequence of arylhydrocarbon receptor (AhR) activation and cytotoxicity, presumably via stimulation of regenerative proliferation (ATSDR, 2004; WHO, 1994, EFSA, 2010).

IARC (1986) has classified PBBs (FireMaster BP-6, 059536-65-1) in group 2B: There is sufficient evidence for the carcinogenicity of commercial mixtures of polybrominated biphenyls to experimental animals; There is inadequate evidence for the carcinogenicity of polybrominated biphenyls to humans.

Endocrine effects
PBBs have been shown to have the potential to affect the endocrine system. Evidence from animal studies indicate that exposure to PBB influences the thyroid hormone homeostasis and reproductive organs, and cause adverse effect on subsequent generations (EFSA, 2010). Animal studies indicate that thyroid hormone homeostatis is a target of PBBs. The observed effects include decreases in serum levels of thyroid hormones (thyroxine (T4) and triiodothyronine (T3)), elevated thyroid stimulating hormone (TSH) levels, thyroid enlargement and morphological changes in follicular cells.
Several studies showed the effects of the exposure to PBBs on sex hormones and adrenal cortex hormones (EFSA, 2010).

PBBs (FireMaster preparations) caused liver enlargement, hepatocellular hypertrophy, fatty degeneration and enzyme induction in experimental animals.

Based on the available data there is evidence that PBBs affect neurobehavioral development and the immune system. These effects occur at slightly higher levels than those on liver and thyroid hormones. Exposure to PBBs during early pregnancy can lead to resorption of foetuses and foetal malformations (EFSA, 2010).

The technical PBB mixtures used in the different toxicity tests comprise both *ortho* and non-*ortho* substituted congeners. The non-*ortho* congeners have been shown to activate the AhR receptor and a number of the toxic effects observed are consistent with dioxin-like activity. There is some evidence that *ortho*-substituted PBB congeners can activate other receptors such as CAR and pregnane X receptor (PXR). Activation of these receptors can lead to increased catabolism of thyroid hormones. The effects on the liver including hepatocarcinogenesis and on the thyroid hormone homeostasis may be a consequence of such receptor activation (EFSA, 2010).

Others effects
PBB congeners have been reported to elicit hepatotoxicity, liver hyperplasia and interference with thyroid hormone regulation, immunotoxicity, teratogenicity and developmental neurobehavioral effects. Due to the structural similarity with PCBs, PBBs share many toxicological properties and structure activity relationships. According to Safe (1984), binding to the AhR, induction of AhR-mediated gene expression and subsequent dioxin-like toxicity is the major toxic mode of action of non-*ortho* PBBs (BB-77, -126 and -169) and mono-*ortho*-brominated congeners and PBB mixtures.

Establishment of Health Based Reference Values
In considering all the different toxicological endpoints affected by PBBs, the CONTAM Panel of EFSA selected the hepatic carcinogenic effects as the critical effect for the derivation of a reference point for gauging the potential health risks of dietary exposure to PBBs. The NOEL for this endpoint is 0.15 mg/kg bw By applying an uncertainty factor of 1,000 to this NOEL, WHO (1984) concluded that the total daily intake from food, water, air and soil should be less than 0.15 µg/kg bw per day.
The CONTAM Panel noted however, that this NOEL represents a worst case situation as it was obtained in a study with a technical PBB mixture (FireMaster FF-1), the congener composition of which is not representative of the congener profiles currently found in food, where the number of congeners detectable is limited. Therefore, the CONTAM Panel concluded that it was inappropriate to use this NOEL to derive a health based guidance value for PBBs.

Occurrence in food

PBBs are present in the environment at low concentrations and likewise in biota and in food and feed (EFSA, 2010).
Jaspers et al. (2005) report on the occurrence of BB-153 in eggs from little owls from Belgium. Based on 39 samples, the concentration of BB153 range from 1 to 6 ng/g fat (mean 2ng/g fat).

The CONTAM Panel of EFSA (2010) focused the analysis of the occurrence data on 16 PBB congeners in food, categories of animal origin: “Fish and other seafood”, “Meat and meat products”, “Animal and vegetable fats and oils”, “Milk and dairy products” and “Food for infants and small children”. This was based on literature data showing that PBBs accumulate in such foods (Gieron et al., 2010; Zabik et al., 1978, 1980; Zabik and Zabik, 1999).

Zabik and Zabik (1999) reviewed the effects of processing and cooking on the levels of PCBs, PBBs and dioxins in food and reported the following observations regarding PBBs:(i) spray drying removed one-quarter of the PBBs from whole milk and one-half of skim milk,(ii) pressure cooking chicken pieces resulted in a 39-57 % PBBs loss and (iii) cooking beef resulted in a one-quarter to one-half loss of PBBs with the high heat of broiling resulting in the higher losses.
Eyster et al. (1983) and Jacobson et al. (1984) showed that PBBs can be transferred across the human placenta and into maternal milk.

Recent data on PBB levels in human milk are scarce. Shen et al. (2008) analyzed human milk samples from Denmark (n=65) and Finland (n=65) for a number of persistent organohalogen compounds, including several PBB congeners. The analyses comprised the following PBB congeners: BB-4, -31, -37, -49, -52, -77, -80, -101, -103, -126, -153, -155 and -169. BB-153 and -155 were the most frequently found congeners with 100 % and 52-77 % samples found positive, respectively. The levels of BB-153 were significantly higher in Danish human milk samples (range: 0.041-1.499, mean: 0.20 ng/g fat) than in the Finnish samples (range: 0.026-1.204, mean: 0.134 ng/g fat). In contrast, the concentrations of the second most frequently found congener, BB-155, were significantly higher in the Finnish human milk samples (range: 0.003-0.060, mean: 0.013 ng/g fat) compared to the Danish samples (range: 0.002-0.049, mean: 0.010 ng/g fat). BB-77 was detected in 61 and 42 % of the Danish and Finnish samples with concentrations of 0.003-0.047 (mean: 0.010) ng/g fat and 0.002-0.027 (mean: 0.009) ng/g fat, respectively. The other PBB congeners were found in less than 30 % of the samples. BB-4, -37, -103 and -126 were not detected in any sample. BB-169 was only found at traces in one sample.

Dietary exposure assessment

Environmental occurrence and human exposure in Europe are due to historical production and use of PBBs (EFSA, 2010).
The highest exposure to PBBs is due to the consumption of fish and other seafood. The median estimated exposure for average consumers across countries of BB-153 is between 0.24 and 5.5 pg/kg bw/day, for lower and upper bound, respectively. Median dietary exposure to BB-52 across countries is between 1.2 and 1.3 pg/kg bw/day for lower and upper bound, followed by BB-101 and -49 with an intake respectively 2 to 3 times and 3 to 4 times lower than BB-52.
For high fish consumers, exposure to BB-153 is estimated to be between 1.2 pg/kg bw/day (lower bound) and 28.2 pg/kg bw/day (upper bound). Exposure to BB-52 is between 6.3 pg/kg bw/day (lower bound) and 6.4 pg/kg bw/day (upper bound). Exposure to BB-101 and -49 is around 2 and 3 times lower than BB-52.
Exposure of children from 1 to 3 years old stems particularly from milk and dairy products with a median average intake for BB-52 and -101 between 0.34 pg/kg bw and 16.1 pg/kg bw/day (lower and upper bound, respectively), and between 0.41 pg/kg bw and 16.2 pg/kg bw (lower and upper bound, respectively).

Exposure of children of 3 to 6 years old mostly stems from the consumption of fish and seafood and of meat and meat products. The consumption of products from these two food categories leads to an average intake of BB-52 and -101 which is almost twice that of adults.

The CONTAM Panel identified a specific group of the population comprising high and frequent fish consumers consuming fatty fish meat (>8 % fat) as those with the highest exposure to PBBs in the

diet of all of the subgroups considered, other than breast-fed infants. The upper bound estimate of exposure to the sum of the 5 PBB congeners (BB-49, -52, -77, -101 and -153) for which the percentage of non detects was less than 80 % is 0.15 ng/kg bw/day (EFSA, 2010).
The mean exposure for infants with high human milk consumption was in the region of 0.9 to 1.4 ng/kg bw per day (EFSA, 2010).
A summary of the dietary sources of PBBS for different groups of the population is shown below. The consumption of food supplements containing special fatty acids would add an additional exposure.

Medians of calculated or reported exposures (pg/kg b.w. per day)						
Exposed population	**Food category**	**PBB congener**	**Average consumers**		**High consumers**	
			LB	**UB**	**LB**	**UB**
Infants	Human milk	BB-153	[620, 920]	[920, 1,400] [(a)]		
Infants	Ready to eat meal	BB-153	0.17, 0.64 [(b)]			
Children 1-3 years	Milk and dairy products	BB-52	0.34	16.1	0.69	32.1
		BB-101	0.41	16.2	0.82	32.3
Children 3-6 years	Fish and other seafood	BB-49	0.76	0.88	3.28	3.79
		BB-52	2.44	2.50	10.4	10.7
		BB-77	0.01	0.01	0.04	0.06
		BB-101	0.90	1.08	3.86	4.63
		BB-153	0.47	11	2.01	47
	Meat and meat products	BB-52	0.23	1.66	0.42	2.97
		BB-101	0.23	1.66	0.42	2.97
Adults	Fish and other seafood	BB-49	0.39	0.45	1.97	2.28
		BB-52	1.23	1.26	6.27	6.45
		BB-77	0.01	0.01	0.03	0.03
		BB-101	0.46	0.54	2.32	2.78
		BB-153	0.24	5.53	1.21	28.2
	Meat and meat products	BB-52	0.10	0.74	0.25	1.76
		BB-101	0.10	0.74	0.25	1.76
	Milk and dairy products	BB-52	0.05	1.91	0.10	4.84
		BB-101	0.04	1.91	0.12	4.86
Adults Specific groups of the population	Fish with more than 8 % fat content; assumed daily intake of 179 g fish meat [(c)]	BB-49			9.61	11.22
		BB-52			34.4	35
		BB-77			0.060	0.090
		BB-101			12.2	14.1
		BB-153			4.33	89
	Supplements containing special fatty acids (e.g. omega-3, essential fatty acids); assumed daily intake of 15 mL (as maximum daily consumption of cod liver oil)[(d)]	BB-49			2.0	10.4
		BB-52			3.0	4.5
		BB-77			0.01	0.02
		BB-101			3.0	4.8
		BB-153			3.8	18.9

b.w.: body weight.
(a): Results reported from a recent study in Finnish and Danish human milk samples, respectively (Shen et al., 2008); the values refer to the mean intake for average and high consumers.
(b): Those estimates refer to two upper bound exposure estimated from the only two available consumption surveys.
(c): Mean exposure estimations based on LB and UB occurrence means reported in Table 8.
(d): Mean exposure estimations based on Table 17.

Risk characterization

The intake of PBBs by high and frequent consumers of fatty fish, the subgroup of the population with the highest dietary exposure, was approximately 6 orders of magnitude less than the NOEL of 0.15 mg/kg bw.
Exposure for high consuming breast-fed infants is 5 orders of magnitude less than this NOEL.

The CONTAM Panel concluded that the risk to the European population from exposure to PBBs through the diet in Europe, even considering the difference in half-lives between rats and humans, is of no concern (EFSA, 2010).

Legislation

PBBs are not regulated in food so far under Regulation1881/2006.
PBB nor other brominated flame retardants are regulated so far by the EU Commission under Directive 2002/32 in feed.
[4]

Recommendations

Since PBBs are no longer produced or used in Europe and taking into account low and declining environmental concentrations, the CONTAM Panel concluded that PBBs are a low priority for further research or monitoring efforts.

The quality assurance for controlling the analytical method should rely on the laboratory's internal measures as there are no certified or standard reference materials available (EFSA, 2010).

Reference

ATSDR (Agency for Toxic Substances and Disease Registry). 2004. Toxicological profile for polybrominated biphenyls and polybrominated diphenyl ethers. U.S. Department of Health and Human Services. Public Health Service. September 2004.

EFSA Panel on Contaminants in the Food Chain (CONTAM). 2010. Scientific Opinion on Polybrominated Biphenyls (PBBs) in Food. The EFSA Journal, 8(10),1789. [151 pp.]. doi:10.2903/j.efsa.2010.1789. Available online: www.efsa.europa.eu

Jaspers V., Covaci A., Maervoet J., Dauwe T., Voorspoels S., Schepens P., Eens M. 2005. Brominated flame retardants and organochlorine pollutants in eggs of little owls (Athene noctua) from Belgium. Environmental Pollution, 136, 81-88.

IARC (International Agency for Research on Cancer). 1986. IARC Monographs on the evaluation of carcinogenic risks to humans. Vol. 41: Some halogenated hydrocarbons and pesticide exposures. World Health Organization, Lyon, France, 261-292.

Luross JM, Alaee M, Sergeant DB, Cannon CM, Whittle DM, Solomon KR and Muir DC, 2002. Spatial distribution of polybrominated diphenyl ethers and polybrominated biphenyls in lake trout from the Laurentian Great Lakes. Chemosphere, 46, 665-672.

NTP (National Toxicology Program). 1993. NTP technical report on the perinatal toxicology and carcinogenesis studies of polybrominated biphenyls (Firemaster FF-1) (CAS No. 67774-32-7) in F344/N rats and B6C3F1 mice (feed studies). Research Triangle Park, NC, US Department of Health and Human Services, National Toxicology Program (NTP TR 398, NIH publication No. 92-2853).

Shen H., Main K.M., Andersson A.M., Damgaard I.N., Virtanen H.E., Skakkebaek N.E., Toppari J., Schramm KW. 2008. Concentrations of persistent organochlorine compounds in human milk and placenta are higher in Denmark than in Finland. Human Reproduction, 23, 201-210.

von der Recke R., Vetter W. 2008. Congener pattern of hexabromobiphenyls in marine biota from different proveniences. The Science of the Total Environment, 393, 358-366.

WHO (World Health Organisation). 1994. International Programme on Chemical Safety (IPCS). Environmental Health Criteria 152. Polybrominated biphenyls. WHO, Geneva.

WHO (World Health Organisation). 1997. Environmental Health Criteria 192. Flame Retardants: A General Introduction. Geneva, Switzerland: International Program on Chemical Safety, World Health Organization.

WHO/IPCS (World Health Organisation/International Program on Chemical Safety), 2008. Uncertainty and data quality in exposure assessment. Part 1: Guidance document on characterizing and communicating uncertainty in exposure assessment. Harmonization Project Document No. 6. ISBN 978 92 4 156376 5.

Zabik M.E., Zabik MJ. 1999. Polychlorinated biphenyls, polybrominated biphenyls, and dioxin reduction during processing/cooking food. In: Impact of Processing on Food Safety. Eds Jackson LS, Knize MG and Morgan JN. Kluwer Academic/Plenum Publishers, New York, 213-231.